

=> file medline

FILE 'MEDLINE' ENTERED AT 12:45:34 ON 30 MAY 2002

FILE LAST UPDATED: 29 MAY 2002 (20020529/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

MEDLINE is now updated 4 times per week. A new current-awareness alert frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> D QUE L7

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L1 ( 345096)SEA FILE=MEDLINE ABB=ON PLU=ON BASE SEQUENCE+NT/CT
L2 ( 17591)SEA FILE=MEDLINE ABB=ON PLU=ON CONSERVED SEQUENCE+NT/CT
L3 ( 17966)SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN INHIBITORS+NT,PFT/CT
      OR ALPHA 1-ANTITRYPSIN/CT
L4 ( 10318)SEA FILE=MEDLINE ABB=ON PLU=ON L3/MAJ
L5 ( 6673)SEA FILE=MEDLINE ABB=ON PLU=ON L4 AND HUMAN/CT
L6 ( 268)SEA FILE=MEDLINE ABB=ON PLU=ON L5 AND L1
L7      2 SEA FILE=MEDLINE ABB=ON PLU=ON L6 AND L2
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=> D QUE L12

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L8 ( 6400)SEA FILE=MEDLINE ABB=ON PLU=ON CONSENSUS SEQUENCE/CT
L9 ( 17966)SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN INHIBITORS+NT,PFT/CT
      OR ALPHA 1-ANTITRYPSIN/CT
L10 ( 10318)SEA FILE=MEDLINE ABB=ON PLU=ON L9/MAJ
L11 ( 6673)SEA FILE=MEDLINE ABB=ON PLU=ON L10 AND HUMAN/CT
L12      0 SEA FILE=MEDLINE ABB=ON PLU=ON L11 AND L8
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=> D QUE L20

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L13 ( 345096)SEA FILE=MEDLINE ABB=ON PLU=ON BASE SEQUENCE+NT/CT
L14 ( 86834)SEA FILE=MEDLINE ABB=ON PLU=ON SEQUENCE HOMOLOGY+NT/CT
L15 ( 17966)SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN INHIBITORS+NT,PFT/CT
      OR ALPHA 1-ANTITRYPSIN/CT
L16 ( 10318)SEA FILE=MEDLINE ABB=ON PLU=ON L15/MAJ
L17 ( 6673)SEA FILE=MEDLINE ABB=ON PLU=ON L16 AND HUMAN/CT
L18 ( 268)SEA FILE=MEDLINE ABB=ON PLU=ON L17 AND L13
L19 ( 1638)SEA FILE=MEDLINE ABB=ON PLU=ON L14/MAJ
L20      2 SEA FILE=MEDLINE ABB=ON PLU=ON L18 AND L19
```

=> D QUE L28

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L21 ( 345096)SEA FILE=MEDLINE ABB=ON PLU=ON BASE SEQUENCE+NT/CT
L22 ( 80566)SEA FILE=MEDLINE ABB=ON PLU=ON NUCLEIC ACID HYBRIDIZATION+NT/CT
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L23 ( 86834) SEA FILE=MEDLINE ABB=ON PLU=ON SEQUENCE HOMOLOGY+NT/CT  
 L24 ( 17966) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN INHIBITORS+NT, PFT/CT  
           OR ALPHA 1-ANTITRYPSIN/CT  
 L25 ( 11446) SEA FILE=MEDLINE ABB=ON PLU=ON L24 AND HUMAN/CT  
 L26 ( 362) SEA FILE=MEDLINE ABB=ON PLU=ON L25 AND L21  
 L27 ( 29) SEA FILE=MEDLINE ABB=ON PLU=ON L26 AND L22  
 L28 5 SEA FILE=MEDLINE ABB=ON PLU=ON L27 AND L23

=> D QUE L33

L29 ( 17591) SEA FILE=MEDLINE ABB=ON PLU=ON CONSERVED SEQUENCE+NT/CT  
 L30 ( 30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN+PFT/CT  
 L31 ( 119) SEA FILE=MEDLINE ABB=ON PLU=ON L30 (L) AI/CT  
 L32 ( 54) SEA FILE=MEDLINE ABB=ON PLU=ON L31 AND HUMAN/CT  
 L33 0 SEA FILE=MEDLINE ABB=ON PLU=ON L32 AND L29

=> D QUE L38

L34 ( 80566) SEA FILE=MEDLINE ABB=ON PLU=ON NUCLEIC ACID HYBRIDIZATION+NT/  
           CT  
 L35 ( 30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN+PFT/CT  
 L36 ( 119) SEA FILE=MEDLINE ABB=ON PLU=ON L35 (L) AI/CT  
 L37 ( 54) SEA FILE=MEDLINE ABB=ON PLU=ON L36 AND HUMAN/CT  
 L38 0 SEA FILE=MEDLINE ABB=ON PLU=ON L37 AND L34

=> D QUE L43

L39 ( 86834) SEA FILE=MEDLINE ABB=ON PLU=ON SEQUENCE HOMOLOGY+NT/CT  
 L40 ( 30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN+PFT/CT  
 L41 ( 119) SEA FILE=MEDLINE ABB=ON PLU=ON L40 (L) AI/CT  
 L42 ( 54) SEA FILE=MEDLINE ABB=ON PLU=ON L41 AND HUMAN/CT  
 L43 0 SEA FILE=MEDLINE ABB=ON PLU=ON L42 AND L39

=> D QUE L48

L44 ( 17966) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN INHIBITORS+NT, PFT/CT  
           OR ALPHA 1-ANTITRYPSIN/CT  
 L45 ( 30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN+PFT/CT  
 L46 ( 119) SEA FILE=MEDLINE ABB=ON PLU=ON L45 (L) AI/CT  
 L47 ( 54) SEA FILE=MEDLINE ABB=ON PLU=ON L46 AND HUMAN/CT  
 L48 11 SEA FILE=MEDLINE ABB=ON PLU=ON L47 AND L44

=> D QUE L54

L49 ( 17966) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN INHIBITORS+NT, PFT/CT  
           OR ALPHA 1-ANTITRYPSIN/CT  
 L50 ( 10318) SEA FILE=MEDLINE ABB=ON PLU=ON L49/MAJ  
 L51 ( 6673) SEA FILE=MEDLINE ABB=ON PLU=ON L50 AND HUMAN/CT  
 L52 ( 30934) SEA FILE=MEDLINE ABB=ON PLU=ON TRYPSIN+PFT/CT  
 L53 ( 119) SEA FILE=MEDLINE ABB=ON PLU=ON L52 (L) AI/CT  
 L54 5 SEA FILE=MEDLINE ABB=ON PLU=ON L51 AND L53

=> S L7 OR L20 OR L28 OR L48 OR L54

L205 20 L7 OR L20 OR L28 OR L48 OR L54

=> FILE CAPLUS

FILE 'CAPLUS' ENTERED AT 12:48:45 ON 30 MAY 2002

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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FILE COVERS 1907 - 30 May 2002 VOL 136 ISS 22  
FILE LAST UPDATED: 29 May 2002 (20020529/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D QUE L58

L55 (	4508)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	TRYPSIN INHIBITOR+PFT/CT
L56 (	302)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	L55 (L) HUMAN
L57 (	113)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	SEQUENCE HOMOLOGY ANALYSIS+PFT/CT
L58	0	SEA FILE=CAPLUS	ABB=ON	PLU=ON	L56 AND L57

=> D QUE L62

L59 (	4508)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	TRYPSIN INHIBITOR+PFT/CT
L60 (	302)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	L59 (L) HUMAN
L61 (	20207)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	NUCLEIC ACID HYBRIDIZATION+NT,P FT/CT
L62	1	SEA FILE=CAPLUS	ABB=ON	PLU=ON	L60 AND L61

=> D QUE L64

L63 (	4508)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	TRYPSIN INHIBITOR+PFT/CT
L64	4	SEA FILE=CAPLUS	ABB=ON	PLU=ON	L63 AND HUMAN/CT

=> D QUE L68

L65 (	113)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	SEQUENCE HOMOLOGY ANALYSIS+PFT/CT
L66 (	16881)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	TRYPSIN+PFT/CT
L67 (	42)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	L66 AND HUMAN/CT
L68	0	SEA FILE=CAPLUS	ABB=ON	PLU=ON	L67 AND L65

=> D QUE L72

L69 (	20207)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	NUCLEIC ACID HYBRIDIZATION+NT,P FT/CT
L70 (	16881)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	TRYPSIN+PFT/CT
L71 (	42)	SEA FILE=CAPLUS	ABB=ON	PLU=ON	L70 AND HUMAN/CT
L72	2	SEA FILE=CAPLUS	ABB=ON	PLU=ON	L71 AND L69

=&gt; D QUE L74

L73 ( 4667) SEA FILE=CAPLUS ABB=ON PLU=ON PROTEINASE INHIBITOR+PFT/CT  
 L74 1 SEA FILE=CAPLUS ABB=ON PLU=ON L73 AND NHP/OBI

=&gt; D QUE L81

L75 ( 4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT  
 L76 ( 113) SEA FILE=CAPLUS ABB=ON PLU=ON SEQUENCE HOMOLOGY ANALYSIS+PFT/  
 CT  
 L77 ( 16881) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN+PFT/CT  
 L78 ( 3233) SEA FILE=CAPLUS ABB=ON PLU=ON L77 (L) (ANTAGONI? OR INHIBIT?)  
 L79 ( 7368) SEA FILE=CAPLUS ABB=ON PLU=ON L75 OR L78  
 L80 ( 8) SEA FILE=CAPLUS ABB=ON PLU=ON L79 AND MAMMAL/CT  
 L81 0 SEA FILE=CAPLUS ABB=ON PLU=ON L76 AND L80

=&gt; D QUE L88

L82 ( 4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT  
 L83 ( 20207) SEA FILE=CAPLUS ABB=ON PLU=ON NUCLEIC ACID HYBRIDIZATION+NT, P  
 FT/CT  
 L84 ( 16881) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN+PFT/CT  
 L85 ( 3233) SEA FILE=CAPLUS ABB=ON PLU=ON L84 (L) (ANTAGONI? OR INHIBIT?)  
 L86 ( 7368) SEA FILE=CAPLUS ABB=ON PLU=ON L82 OR L85  
 L87 ( 8) SEA FILE=CAPLUS ABB=ON PLU=ON L86 AND MAMMAL/CT  
 L88 0 SEA FILE=CAPLUS ABB=ON PLU=ON L87 AND L83

=&gt; D QUE L92

L89 ( 4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT  
 L90 ( 113) SEA FILE=CAPLUS ABB=ON PLU=ON SEQUENCE HOMOLOGY ANALYSIS+PFT/  
 CT  
 L91 ( 23) SEA FILE=CAPLUS ABB=ON PLU=ON L89 (L) MAMMA?  
 L92 0 SEA FILE=CAPLUS ABB=ON PLU=ON L91 AND L90

=&gt; D QUE L96

L93 ( 4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT  
 L94 ( 20207) SEA FILE=CAPLUS ABB=ON PLU=ON NUCLEIC ACID HYBRIDIZATION+NT, P  
 FT/CT  
 L95 ( 23) SEA FILE=CAPLUS ABB=ON PLU=ON L93 (L) MAMMA?  
 L96 0 SEA FILE=CAPLUS ABB=ON PLU=ON L95 AND L94

=&gt; D QUE L106

L97 ( 4508) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN INHIBITOR+PFT/CT  
 L98 ( 302) SEA FILE=CAPLUS ABB=ON PLU=ON L97 (L) HUMAN  
 L99 ( 4) SEA FILE=CAPLUS ABB=ON PLU=ON L97 AND HUMAN/CT  
 L100 ( 16881) SEA FILE=CAPLUS ABB=ON PLU=ON TRYPSIN+PFT/CT  
 L101 ( 3233) SEA FILE=CAPLUS ABB=ON PLU=ON L100 (L) (ANTAGONI? OR  
 INHIBIT?)  
 L102 ( 7368) SEA FILE=CAPLUS ABB=ON PLU=ON L97 OR L101  
 L103 ( 8) SEA FILE=CAPLUS ABB=ON PLU=ON L102 AND MAMMAL/CT  
 L104 ( 23) SEA FILE=CAPLUS ABB=ON PLU=ON L97 (L) MAMMA?  
 L105 ( 325) SEA FILE=CAPLUS ABB=ON PLU=ON L98 OR L99 OR L103 OR L104  
 L106 7 SEA FILE=CAPLUS ABB=ON PLU=ON L105 AND (HOMOLOG?/OBI OR  
 ORTHOLOG?/OBI OR PARALOG?/OBI OR SEQUENCE/OBI (W) SIMILARITY/OB

I)

=> S L62 OR L64 OR L72 OR L74 OR L106  
 L206 14 L62 OR L64 OR L72 OR L74 OR L106

=> FILE EMBASE

FILE 'EMBASE' ENTERED AT 12:51:49 ON 30 MAY 2002

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FILE COVERS 1974 TO 23 May 2002 (20020523/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate  
 substance identification.

=> D QUE L111

L107(	3032)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	CONSENSUS SEQUENCE+PFT/CT
L108(	15195)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	TRYPSIN INHIBITOR+NT,PFT/CT
L109(	10579)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L108 /MAJ
L110(	4459)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L109 AND HUMAN/CT
L111	2	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L110 AND L107

=> D QUE L118

L112(	75645)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	NUCLEOTIDE SEQUENCE+PFT/CT
L113(	41190)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	SEQUENCE HOMOLOGY+PFT/CT
L114(	15195)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	TRYPSIN INHIBITOR+NT,PFT/CT
L115(	10579)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L114 /MAJ
L116(	4459)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L115 AND HUMAN/CT
L117(	28)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L116 AND L112
L118	4	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L117 AND L113

=> D QUE L123

L119(	54)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	ORTHOLOGY+PFT/CT
L120(	15195)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	TRYPSIN INHIBITOR+NT,PFT/CT
L121(	10579)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L120 /MAJ
L122(	4459)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L121 AND HUMAN/CT
L123	0	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L122 AND L119

=> D QUE L128

L124(	3032)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	CONSENSUS SEQUENCE+PFT/CT
L125(	15195)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	TRYPSIN INHIBITOR+NT,PFT/CT
L126(	2307)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L125 (L) EC/CT
L127(	1823)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L126 AND HUMAN/CT
L128	2	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L127 AND L124

=> D QUE L135

L129(	75645)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	NUCLEOTIDE SEQUENCE+PFT/CT
L130(	41190)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	SEQUENCE HOMOLOGY+PFT/CT
L131(	15195)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	TRYPSIN INHIBITOR+NT,PFT/CT
L132(	2307)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L131 (L) EC/CT
L133(	1823)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L132 AND HUMAN/CT
L134(	19)	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L133 AND L129
L135	4	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L134 AND L130

=> D QUE L140

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L136(      54)SEA FILE=EMBASE ABB=ON  PLU=ON  ORTHOLOGY+PFT/CT
L137(    15195)SEA FILE=EMBASE ABB=ON  PLU=ON  TRYPSIN INHIBITOR+NT,PFT/CT
L138(     2307)SEA FILE=EMBASE ABB=ON  PLU=ON  L137 (L) EC/CT
L139(     1823)SEA FILE=EMBASE ABB=ON  PLU=ON  L138 AND HUMAN/CT
L140         0 SEA FILE=EMBASE ABB=ON  PLU=ON  L139 AND L136
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=> D QUE L148

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L141(    63010)SEA FILE=EMBASE ABB=ON  PLU=ON  PROTEINASE INHIBITOR+NT/CT
L142(    75645)SEA FILE=EMBASE ABB=ON  PLU=ON  NUCLEOTIDE SEQUENCE+PFT/CT
L143(     685)SEA FILE=EMBASE ABB=ON  PLU=ON  L141 AND L142
L144(   39777)SEA FILE=EMBASE ABB=ON  PLU=ON  L141/MAJ
L145(     408)SEA FILE=EMBASE ABB=ON  PLU=ON  L144 AND L142
L146(     54)SEA FILE=EMBASE ABB=ON  PLU=ON  ORTHOLOGY+PFT/CT
L147(      1)SEA FILE=EMBASE ABB=ON  PLU=ON  L143 AND L146
L148         0 SEA FILE=EMBASE ABB=ON  PLU=ON  L145 AND L147
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=> S L111 OR L118 OR L128 OR L135

L207 7 L111 OR L118 OR L128 OR L135

=> FILE USPATFUL

FILE 'USPATFULL' ENTERED AT 12:57:03 ON 30 MAY 2002  
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 28 May 2002 (20020528/PD)  
FILE LAST UPDATED: 28 May 2002 (20020528/ED)  
HIGHEST GRANTED PATENT NUMBER: US6397388  
HIGHEST APPLICATION PUBLICATION NUMBER: US2002062508  
CA INDEXING IS CURRENT THROUGH 28 May 2002 (20020528/UPCA)  
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 28 May 2002 (20020528/PD)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2002  
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2002

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>>> USPAT2 is now available.  USPATFULL contains full text of the  <<<
>>> original, i.e., the earliest published granted patents or  <<<
>>> applications.  USPAT2 contains full text of the latest US  <<<
>>> publications, starting in 2001, for the inventions covered in  <<<
>>> USPATFULL.  A USPATFULL record contains not only the original  <<<
>>> published document but also a list of any subsequent  <<<
>>> publications.  The publication number, patent kind code, and  <<<
>>> publication date for all the US publications for an invention  <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL  <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc.  <<<
```

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>>> USPATFULL and USPAT2 can be accessed and searched together  <<<
>>> through the new cluster USPATALL.  Type FILE USPATALL to  <<<
>>> enter this cluster.  <<<
>>>  <<<
>>> Use USPATALL when searching terms such as patent assignees,  <<<
>>> classifications, or claims, that may potentially change from  <<<
>>> the earliest to the latest publication.  <<<
```

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> D QUE L150

L149( 35)SEA FILE=USPATFULL ABB=ON PLU=ON (TRYPSIN/TI (3A) (INHIBIT?/T  
I OR ANTAGONI?/TI))  
L150 3 SEA FILE=USPATFULL ABB=ON PLU=ON L149 AND (MAMMA?/TI OR  
HUMAN/TI)

=> D QUE L154

L151( 38417)SEA FILE=USPATFULL ABB=ON PLU=ON (MAMMA?/AB OR HUMAN/AB)  
L152( 139)SEA FILE=USPATFULL ABB=ON PLU=ON (TRYPSIN/AB (3A) (INHIBIT?/A  
B OR ANTAGONI?/AB))  
L153( 52456)SEA FILE=USPATFULL ABB=ON PLU=ON (ORTHOLOG?/AB OR HOMOLOG?/AB  
OR SIMILAR?/AB OR IDENTITY/AB OR PARALOG?/AB)  
L154 4 SEA FILE=USPATFULL ABB=ON PLU=ON L151 AND L152 AND L153

=> D QUE L160

L155( 1012)SEA FILE=USPATFULL ABB=ON PLU=ON ((PROTEINASE/AB OR PROTEASE/  
AB) (3A) (INHIBIT?/AB OR ANTAGONI?/AB))  
L156( 38417)SEA FILE=USPATFULL ABB=ON PLU=ON (MAMMA?/AB OR HUMAN/AB)  
L157( 356)SEA FILE=USPATFULL ABB=ON PLU=ON (TRYPSIN/AB)  
L158( 16)SEA FILE=USPATFULL ABB=ON PLU=ON L155 AND L157 AND L156  
L159( 50684)SEA FILE=USPATFULL ABB=ON PLU=ON SEQUENC?/AB  
L160 3 SEA FILE=USPATFULL ABB=ON PLU=ON L158 AND L159

=> D QUE L168

L161( 1842944)SEA FILE=USPATFULL ABB=ON PLU=ON ORTHOLOG? OR HOMOLOG? OR  
SIMILAR? OR IDENTITY OR PARALOG?  
L162( 1012)SEA FILE=USPATFULL ABB=ON PLU=ON ((PROTEINASE/AB OR PROTEASE/  
AB) (3A) (INHIBIT?/AB OR ANTAGONI?/AB))  
L163( 38417)SEA FILE=USPATFULL ABB=ON PLU=ON (MAMMA?/AB OR HUMAN/AB)  
L164( 356)SEA FILE=USPATFULL ABB=ON PLU=ON (TRYPSIN/AB)  
L165( 16)SEA FILE=USPATFULL ABB=ON PLU=ON L162 AND L164 AND L163  
L166( 14)SEA FILE=USPATFULL ABB=ON PLU=ON L165 AND L161  
L167( 12008)SEA FILE=USPATFULL ABB=ON PLU=ON (PROTEIN OR PEPTIDE)/TI  
L168 2 SEA FILE=USPATFULL ABB=ON PLU=ON L166 AND L167

=> S L150 OR L154 OR L160 OR L168

L208 12 L150 OR L154 OR L160 OR L168

=> FILE WPIDS

FILE 'WPIDS' ENTERED AT 12:59:47 ON 30 MAY 2002  
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FILE LAST UPDATED: 28 MAY 2002 <20020528/UP>  
MOST RECENT DERWENT UPDATE 200234 <200234/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> The BATCH option for structure searches has been  
enabled in WPINDEX/WPIDS and WPIX >>>

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,  
SEE <http://www.derwent.com/dwpi/updates/dwpcov/index.html> <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX TOOLS OF THE  
TRADE USER GUIDE, PLEASE VISIT:

<http://www.derwent.com/data/stn3.pdf> <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER  
GUIDES, PLEASE VISIT:  
[http://www.derwent.com/userguides/dwpi\\_guide.html](http://www.derwent.com/userguides/dwpi_guide.html) <<<

=> D QUE L173

L169( 781)SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR  
ANTAG?)  
L170( 133029)SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?  
L171( 74)SEA FILE=WPIDS ABB=ON PLU=ON L169 (3A) L170  
L172( 11423)SEA FILE=WPIDS ABB=ON PLU=ON HOMOLOG? OR ORTHOLOG? OR  
PARALOG? OR SEQUENCE (W) SIMILARITY  
L173 1 SEA FILE=WPIDS ABB=ON PLU=ON L171 AND L172

=> D QUE L180

L174( 781)SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR  
ANTAG?)  
L175( 133029)SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?  
L176( 11423)SEA FILE=WPIDS ABB=ON PLU=ON HOMOLOG? OR ORTHOLOG? OR  
PARALOG? OR SEQUENCE (W) SIMILARITY  
L177( 27100)SEA FILE=WPIDS ABB=ON PLU=ON (NUCLEOTIDE OR NUCLEIC OR DNA  
OR RNA OR GENETIC OR CHROMOSOMAL) (3A) SEQUENC?  
L178( 168)SEA FILE=WPIDS ABB=ON PLU=ON L174 (S) L175  
L179( 8)SEA FILE=WPIDS ABB=ON PLU=ON L178 AND L176  
L180 7 SEA FILE=WPIDS ABB=ON PLU=ON L179 AND L177

=> D QUE L185

L181( 781)SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR  
ANTAG?)  
L182( 133029)SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?  
L183( 74)SEA FILE=WPIDS ABB=ON PLU=ON L181 (3A) L182  
L184( 27100)SEA FILE=WPIDS ABB=ON PLU=ON (NUCLEOTIDE OR NUCLEIC OR DNA  
OR RNA OR GENETIC OR CHROMOSOMAL) (3A) SEQUENC?  
L185 2 SEA FILE=WPIDS ABB=ON PLU=ON L183 AND L184

=> D QUE L189

L186( 781)SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR  
ANTAG?)  
L187( 133029)SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?  
L188( 74)SEA FILE=WPIDS ABB=ON PLU=ON L186 (3A) L187  
L189 1 SEA FILE=WPIDS ABB=ON PLU=ON L188 AND CDNA

=> D QUE L193

L190( 781)SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR  
ANTAG?)  
L191( 133029)SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?  
L192( 168)SEA FILE=WPIDS ABB=ON PLU=ON L190 (S) L191  
L193 4 SEA FILE=WPIDS ABB=ON PLU=ON L192 AND CDNA

=> D QUE L198

L194( 781)SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR  
ANTAG?)  
L195( 133029)SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?  
L196( 74)SEA FILE=WPIDS ABB=ON PLU=ON L194 (3A) L195



L197( 17730)SEA FILE=WPIDS ABB=ON PLU=ON HYBRIDIZ? OR HYBRIDIS?  
L198 1 SEA FILE=WPIDS ABB=ON PLU=ON L196 AND L197

=> D QUE L203

L199( 781)SEA FILE=WPIDS ABB=ON PLU=ON TRYPSIN (3A) (INHIBIT? OR  
ANTAG?)  
L200( 133029)SEA FILE=WPIDS ABB=ON PLU=ON HUMAN OR MAMMA?  
L201( 168)SEA FILE=WPIDS ABB=ON PLU=ON L199 (S) L200  
L202( 17730)SEA FILE=WPIDS ABB=ON PLU=ON HYBRIDIZ? OR HYBRIDIS?  
L203 6 SEA FILE=WPIDS ABB=ON PLU=ON L201 AND L202

=> S L173 OR L180 OR L185 OR L189 OR L193 OR L198 OR L203  
L209 15 L173 OR L180 OR L185 OR L189 OR L193 OR L198 OR L203

=> DUP REM L205-209

FILE 'MEDLINE' ENTERED AT 13:04:14 ON 30 MAY 2002

FILE 'CAPLUS' ENTERED AT 13:04:14 ON 30 MAY 2002  
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FILE 'EMBASE' ENTERED AT 13:04:14 ON 30 MAY 2002  
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FILE 'USPATFULL' ENTERED AT 13:04:14 ON 30 MAY 2002  
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIDS' ENTERED AT 13:04:14 ON 30 MAY 2002  
COPYRIGHT (C) 2002 THOMSON DERWENT  
PROCESSING COMPLETED FOR L205  
PROCESSING COMPLETED FOR L206  
PROCESSING COMPLETED FOR L207  
PROCESSING COMPLETED FOR L208  
PROCESSING COMPLETED FOR L209  
L210 67 DUP REM L205-209 (1 DUPLICATE REMOVED)

=> D IBIB AB 1-67

L210 ANSWER 1 OF 67 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:256312 CAPLUS  
DOCUMENT NUMBER: 136:289989  
TITLE: Protein and cDNA sequences of a novel human trypsin  
sequence homolog and uses thereof  
INVENTOR(S): Meyers, Rachel A.  
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 126 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026802	A2	20020404	WO 2001-US29904	20010924
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,  
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,  
 US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-235023P P 20000925

AB The invention provides protein and cDNA sequences of a novel human protein, designated m32404, which has sequence homol. with trypsin members. The invention also provides antisense nucleic acid mols., recombinant expression vectors contg. m32404 nucleic acid mols., host cells into which the expression vectors have been introduced, and nonhuman transgenic animals in which an m32404 gene has been introduced or disrupted. The invention still further provides isolated m32404 proteins, fusion proteins, antigenic peptides and anti-m32404 antibodies. Diagnostic methods utilizing compns. of the invention are also provided.

L210 ANSWER 2 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:143003 CAPLUS

DOCUMENT NUMBER: 136:180179

TITLE: Methods for ultra-sensitive detection systems

INVENTOR(S): Chait, Brian T.; Latimer, Darin R.; Lizardi, Paul M.;  
 Kershnar, Eric R.; Morrow, Jon S.; Roth, Matthew E.;  
 Mattessich, Martin J.; McConnel, Kevin J.

PATENT ASSIGNEE(S): Agilix Corporation, USA

SOURCE: PCT Int. Appl., 341 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014867	A2	20020221	WO 2001-US41709	20010813
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2000-224939P P 20000811

US 2001-283498P P 20010412

AB Disclosed are compns. and methods for sensitive detection of one or multiple analytes. In general, the methods involve the use of special label components, referred to as reporter signals, that can be assocd. with, incorporated into, or otherwise linked to the analytes. In some embodiments, the reporter signals can be altered such that the altered forms of different reporter signals can be distinguished from each other. In some embodiments, sets of reporter signals can be distinguished from each other. In some embodiments, sets of reporter signals can be used where two or more of the reporter signals in a set have one or more common properties that allow the reporter signals having the common property to be distinguished and/or sepd. from other mols. lacking the common property. In other embodiments, sets of reporter signal/analyte conjugates can be used where two or more of the reporter signal/analyte

conjugates in a set have one or more common properties that allow the reporter signal/analyte conjugates having the common property to be distinguished and/or sepd. from other mols. lacking the common property. Reporter signals can also be in conjunction with analytes (such as in mixts. of reporter signals and analytes), where no significant phys. assocn. between the reporter signals and analytes occurs; or alone, where no analyte is present.

L210 ANSWER 3 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:51264 CAPLUS  
DOCUMENT NUMBER: 136:112690  
TITLE: Method of modulating expression of  
LDL-receptor-related protein and uses thereof  
INVENTOR(S): Partridge, Nicola  
PATENT ASSIGNEE(S): Saint Louis University, USA  
SOURCE: PCT Int. Appl., 67 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003985	A1	20020117	WO 2001-US18919	20010613
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2000-612533 A 20000707

AB Methods for increasing expression of the LDL receptor-related protein (LRP) in cells or animals are disclosed. The methods comprise treating the cells or animals with an HMG-CoA reductase inhibitor (statin). Such treatments are also useful for: reducing activity of LRP ligands in cells or animals, detg. whether a particular condition is caused by insufficient or excess expression of an LRP, detg. whether a particular protein is inactivated by an LRP, and other similar applications. More specifically, the invention relates to the enhancement of levels of LRP in cells and animals and uses thereof in treating disorders mediated by excessive levels of proteins which bind to LRP or have receptors which bind to LRP.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L210 ANSWER 4 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:284646 CAPLUS  
DOCUMENT NUMBER: 136:306664  
TITLE: Antistreptococcal agents containing bactericidal peptides and sterilization of streptococci  
INVENTOR(S): Nishimura, Eisaku; Kato, Masatoshi; Etou, Akiko; Imai, Susumu; Nishizawa, Toshiki; Hanada, Nobuhiro  
PATENT ASSIGNEE(S): Morinaga and Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002114704	A2	20020416	JP 2000-300693	20000929

AB Streptococci are sterilized using agents contg. antibacterial peptides such as human .beta.-defensin-2 and optionally protease inhibitors. The antistreptococcal agents are useful as pharmaceuticals and as food additives. Human .beta.-defensin-2 inhibited growth of Streptococcus gordonii, S. cricetus, S. pyogenes, etc. Combined use of 3,4-dichloroisocoumarin (serine protease inhibitor) enhanced antibacterial activity of human .beta.-defensin-2 on S. anginosus and S. mitis.

L210 ANSWER 5 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-227151 [28] WPIDS

DOC. NO. CPI: C2002-069183

TITLE: gcpE nucleic acid which is an essential gene of the methyl-D-erythritol phosphate pathway, encoding a fully defined GCPE protein which is useful for increasing levels of tocopherol substrates in plants.

DERWENT CLASS: C06 D16

INVENTOR(S): BORONAT, A; CAMPOS, N; RODRIGUEZ-CONCEPCION, M; ROHMER, M; SEEMAN, M; VALENTIN, H E; VENKATESH, T V; VENKATRAMESH, M

PATENT ASSIGNEE(S): (MONS) MONSANTO TECHNOLOGY LLC

COUNTRY COUNT: 95

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002012478	A2	20020214	(200228)*	EN	155

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU  
SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002012478	A2	WO 2001-US24335	20010806

PRIORITY APPLN. INFO: US 2000-223483P 20000807

AB WO 200212478 A UPAB: 20020502

NOVELTY - A substantially purified gcpE nucleic acid molecule (an essential gene of methyl-D-erythritol phosphate (MEP) pathway) (I) that encodes rice, Arabidopsis thaliana, rice or Escherichia coli GCPE protein comprising fully defined 686, 740, 603 or 372 amino acids respectively as given in specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a recombinant nucleic acid molecule (II) as operably linked components:

(a) an exogenous promoter; and

(b) a heterologous nucleic acid molecule encoding rice (S2,9,), A. thaliana (S1,5,13-20,), E. Coli (S3,), soybean (S6,33-46), tomato (S7),

Mesembryanthemum crystallinum (S8), maize (S10,21-32), Loblolly pine (S11), Physcomitrella patens (S12), or Brassica napus (S47) GCPE having fully defined 211-33675 **nucleotide sequences** given in the specification;

(2) a recombinant nucleic acid molecule (III) comprising as operably linked components:

(a) a promoter that functions in a plant cell to cause production of an mRNA molecule, and;

(b) a **nucleic acid sequence** that **hybridizes** under moderate stringency conditions to (S1)-(S3), (S5)-(S47) or their complements, i.e., has greater than 85% identity to the above mentioned sequences or their complements;

(3) a transformed cell (IV) comprising (II);

(4) a substantially purified protein (V) comprising an amino acid sequence of (S4), (S48) or (S49);

(5) an antibody (VI) that specifically binds to (V);

(6) a transgenic plant (VII) comprising (II);

(7) a transgenic plant (VIII) comprising a nucleic acid molecule that encodes GCPE protein, where the nucleic acid molecule comprises a promoter operably linked to heterologous **nucleic acid sequences** having a sequence of (S1)-(S3), (S5)-(S47), or their complements;

(8) a seed (IX) derived from (VII);

(9) oil or meal derived from (IX);

(10) a container (X) of seeds, where at least 25% of the seeds are derived from (VIII); and

(11) feed stock or plant part (XI) derived from (VIII).

USE - (I) having a sequence of (S1)-(S3), (S5)-(S47), and encoding a GCPE protein having a sequence of (S4), (S48)-(S50), is useful for producing a transgenic plant such as Brassica campestris, B.napus, canola, castor bean, coconut, cotton, crambe, linseed, maize, mustard, oil palm, peanut, rapeseed, rice, safflower, sesame, soybean, sunflower, or wheat with an increased isoprenoid (preferably, tocopherol) compound level (claimed). The expression of GCPE protein in organisms increases the level of tocopherol substrate such as isopentyl diphosphate and dimethylallyl diphosphate biosynthesis. Transgenic organisms overexpressing GCPE protein can nutritionally enhance food and feed sources. Overexpression of GCPE protein in transgenic plant may provide tolerance to stresses e.g., oxidative stress tolerance such as to oxygen or ozone, UV tolerance, etc. (I) may be used to obtain nucleic acid molecules from the same species, and to obtain nucleic acid **homologs**. (I) is also used as or primers. The recombinant vectors are used in plant transformation or transfection. (I) can also act as markers capable of detecting polymorphisms such as single nucleotide polymorphisms (SNPs). (I) is also used to determine the level or pattern of expression the protein.

Dwg.0/5

L210 ANSWER 6 OF 67	CAPLUS	COPYRIGHT 2002 ACS	DUPLICATE 1
ACCESSION NUMBER:	2001:636220 CAPLUS		
DOCUMENT NUMBER:	135:206487		
TITLE:	Twelve human polypeptides and their nucleic acids sequences and diagnostic and therapeutic applications		
INVENTOR(S):	Vernet, Corine A. M.; Fernandes, Elma; Shimkets, Richard A.; Macdougall, John; Spaderna, Steven K.		
PATENT ASSIGNEE(S):	Curagen Corporation, USA		
SOURCE:	PCT Int. Appl., 189 pp.		
	CODEN: PIXXD2		
DOCUMENT TYPE:	Patent		
LANGUAGE:	English		
FAMILY ACC. NUM. COUNT:	1		
PATENT INFORMATION:			

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062928	A2	20010830	WO 2001-US6151	20010226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-184951P	P 20000225
			US 2000-185548P	P 20000228
			US 2000-185967P	P 20000301
			US 2000-197723P	P 20000418
			US 2000-199957P	P 20000427
			US 2001-789390	A2 20010223
AB The present invention provides 12 novel human NOVX polynucleotides and polypeptides encoded by the NOVX polynucleotides. Three of the proteins are novel KIAA1233-like polypeptides; four are STE20-like splice variant polypeptides; and five are trypsin inhibitor-like polypeptides. Quant. expression anal. in various cells and tissues suggest that these polypeptide and cDNA mols. may be of value for the diagnosis and treatment of cancer or inflammation conditions. Also provided are the antibodies that immunospecifically bind to a NOVX polypeptide or any deriv., variant, mutant or fragment of the NOVX polypeptide, polynucleotide or antibody. The invention addnl. provides methods in which the NOVX polypeptide, polynucleotide and antibody are utilized in the detection and treatment of a broad range of pathol. states, as well as to other uses.				
L210 ANSWER 7 OF 67 CAPLUS COPYRIGHT 2002 ACS				
ACCESSION NUMBER:		2001:228919 CAPLUS		
DOCUMENT NUMBER:		134:247996		
TITLE:		Protein and cDNA sequences for a novel human protease inhibitor-like protein <b>NHP</b> and use thereof		
INVENTOR(S):		Donoho, Gregory; Turner, C. Alexander, Jr.; Wattler, Frank; Nehls, Michael; Friedrich, Glenn; Zambrowicz, Brian; Sands, Arthur T.		
PATENT ASSIGNEE(S):		Lexicon Genetics Incorporated, USA		
SOURCE:		PCT Int. Appl., 29 pp. CODEN: PIXXD2		
DOCUMENT TYPE:		Patent		
LANGUAGE:		English		
FAMILY ACC. NUM. COUNT:		1		
PATENT INFORMATION:				

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021651	A2	20010329	WO 2000-US26048	20000922
WO 2001021651	A3	20020314		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,				

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 PRIORITY APPLN. INFO.: US 1999-156101P P 19990924  
 AB The invention provides protein and cDNA sequences for a novel human  
 protease inhibitor-like protein NHP that can be used in therapeutic,  
 diagnostic, and pharmacogenomic applications.

L210 ANSWER 8 OF 67 USPATFULL  
 ACCESSION NUMBER: 2001:163313 USPATFULL  
 TITLE: **Protein** having proteinase inhibitor activity  
 INVENTOR(S): Delaria, Kathy, Walnut Creek, CA, United States  
 Rocznia, Steve, Lafayette, CA, United States  
 Davies, Christopher, Walnut Creek, CA, United States  
 PATENT ASSIGNEE(S): Bayer Corporation, Berkeley, CA, United States (U.S.  
 corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6294648	B1	20010925
APPLICATION INFO.:	US 1999-358569		19990720 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	GRANTED		
PRIMARY EXAMINER:	Nashed, Nashaat T.		
ASSISTANT EXAMINER:	Fronza, Christian L		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1188		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB BTL.009 is a novel **human serine proteinase inhibitor** of the Kunitz family that exhibits greater potency towards neutral serine proteinases, particularly leukocyte elastase, and chymotrypsin than towards **trypsin**-like proteinases. BTL.009, or variants thereof, may be employed as therapeutics in diseases such as emphysema, idiopathic pulmonary fibrosis, adult respiratory distress syndrome, cystic fibrosis, rheumatoid arthritis, organ failure, and glomerulonephritis in which uncontrolled proteolysis due to neutral serine proteinase activity results in tissue damage.

L210 ANSWER 9 OF 67 USPATFULL  
 ACCESSION NUMBER: 2001:14463 USPATFULL  
 TITLE: **Protein** having proteinase inhibitor activity  
 INVENTOR(S): Davies, Christopher, 265 San Antonio Way, Walnut Creek,  
 CA, United States 94598  
 Chen, Dadong, 2123 Clinton Ave., #A, Alameda, CA,  
 United States 94501  
 Rocznia, Steve, 11 Hidden Valley Rd., Lafayette, CA,  
 United States 94549

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6180607	B1	20010130
APPLICATION INFO.:	US 1999-369494		19990805 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Wax, Robert A.		
ASSISTANT EXAMINER:	Kerr, Kathleen M.		
LEGAL REPRESENTATIVE:	Beck, Michael J.		
NUMBER OF CLAIMS:	16		
EXEMPLARY CLAIM:	1,11		
LINE COUNT:	1175		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB BTL.010 is a novel **human serine proteinase inhibitor** of the Kunitz family that exhibits greater potency towards neutral serine proteinases, particularly leukocyte elastase-, and proteinase 3, than towards **trypsin**-like proteinases. BTL.010, or variants thereof, may be employed as therapeutics in diseases such as emphysema, idiopathic pulmonary fibrosis, adult respiratory distress syndrome, cystic fibrosis, rheumatoid arthritis, organ failure, and glomerulonephritis in which uncontrolled proteolysis due to neutral serine proteinase activity results in tissue damage.

L210 ANSWER 10 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 2001-582099 [65] WPIDS  
 DOC. NO. NON-CPI: N2001-433669  
 DOC. NO. CPI: C2001-172594  
 TITLE: New stable chloroplast expression vector for introducing multiple genes into a plant by a single integration event, comprises a multi-gene operon which is functional to co-express multiple enzymes in plastids.  
 C06 D16 P13  
 DERWENT CLASS:  
 INVENTOR(S): DANIELL, H; MOAR, W  
 PATENT ASSIGNEE(S): (AUBU) UNIV AUBURN; (UYFL-N) UNIV CENT FLORIDA  
 COUNTRY COUNT: 95  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001064024	A1	20010907	(200165)*	EN	72
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001045360	A	20010912	(200204)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001064024	A1	WO 2001-US6276	20010228
AU 2001045360	A	AU 2001-45360	20010228

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001045360	A Based on	WO 200164024

PRIORITY APPLN. INFO: US 2001-266121P 20010202; US 2000-185660P  
 20000229; US 2000-257408P 20001220; US  
 2000-259248P 20001229

AB WO 200164024 A UPAB: 20011108  
 NOVELTY - A stable chloroplast transformation and expression vector (I) which is capable of introducing multiple genes into a plant by a single integration event, comprises a heterologous coding sequence comprising an expression cassette which comprises a promoter operative in plastids, a selectable marker, multi-gene operon which is functional to co-express multiple enzymes in the plastids, is new.

DETAILED DESCRIPTION - A new stable chloroplast transformation and expression vector (I) comprises a heterologous **DNA**



**sequence** which comprises an expression cassette, comprising operably linked components, in the 5' to the 3' direction of translation, a promoter operative in the plastids which drives a multi-gene operon, a selectable marker sequence, the multi-gene operon which is functional to co-express multiple enzymes in the plastids, a transcription termination region functional in the plastids, and flanking each side of the expression cassette, flanking **DNA sequences** which are **homologous** to **DNA sequences** inclusive of a spacer sequence of the target plastid genome, whereby stable integration of the heterologous coding sequence into the chloroplast genome of the target plant is facilitated throughout **homologous** recombination of the flanking sequence with the **homologous** sequences in the target plastid gene.

INDEPENDENT CLAIMS are also included for the following:

(1) transforming (M1) a chloroplast of a selected plant species or its progeny to confer insect resistance and producing foreign protein on a large scale, involving stably transforming the chloroplast of the selected plant cells to express an insecticidal toxic protein and a chaperonin and growing the transformed plant cells under conditions which allow the expression of the insecticidal toxin protein and chaperonin;

(2) a transformed plant (II) which has been transformed by (M1);

(3) progeny including seeds of (II);

(4) transforming (M2) a chloroplast of a selected plant species or its progeny to confer greater resistance to metal ions than the corresponding parental plant which does not require several back crosses to create a complete pathway that detoxifies mercury and organomercurial compounds involving stably transforming the chloroplast of a plant by inserting an expression cassette containing (I), where the expression cassette comprises the mercury resistance coding sequences that encode Mer A and Mer B enzymes, into a plant species or its progeny and growing the transforming plant species under conditions which allow the expression of the expression cassette;

(5) a stably transformed plant (III) which has been transformed by (M2);

(6) progeny including seeds of stably transformed (III);

(7) phytoremediation (M3) which does not require several backcrosses to create a complete pathway that detoxifies mercury and organomercurial comprising (M2);

(8) a photosynthetic organism (IV) transformed with (I) where the expression cassette comprises genes for a biosynthetic pathway that is a bioremediation system functioning to degrade inorganic and organic mercury compounds, and where (IV) is useful for bioremediation of mercury and organomercuric compounds from contaminated water bodies; and

(9) transforming (M4) a chloroplast of a selected photosynthetic organism to confer greater resistance to metal ions involving stably transforming chloroplast with (I) where the expression cassette comprises genes for a biosynthetic pathway that is a bioremediation system functioning to degrade inorganic and organic mercury compounds, and growing the transformed photosynthetic organism which allows the expression of the expression cassette.

ACTIVITY - Anti-insecticidal. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - (I) is useful in a bioremediation process where its expression cassette comprises operon having genes that function to degrade inorganic compounds such as divalent cations of mercury, nickel, cobalt, trivalent cations of gold, or monovalent cations of silver, and organic compounds such as alkyl mercury, alkenyl mercury, alkynyl mercury, aromatic mercury compounds, alkyl lead compounds, alkyl arsenic compounds or alkyl cadmium compounds. A transformed plant (III) or its progeny including seeds is useful for phytoremediation of mercury and organomercurials in soil and

ground waters. The method involves planting (III) or progeny in soils contaminated with organomercurials and allowing the plants to grow. A photosynthetic organism (IV) transformed with (I) is useful for phytoremediation of mercury and organomercurials in contaminated water which involves treating water contaminated with the mercury with (IV) before releasing the water into the environment. (IV) is a green algae such as *Chlorella vulgaris* or a cyanobacteria such as *Synechocystis* (claimed). The vector is useful for genetic engineering of plant cells, preferably for engineering novel pathways for metabolic engineering and gene stacking. The mer operon-expressing plants can be used in remediation of mercury-contaminated soil to block the biomagnification of methyl mercury up the food chain.

**ADVANTAGE** - The vector provides enhanced expression of several foreign proteins in plastids utilizing a single transformation event. Blocks of foreign genes in the single operon avoids complications inherent in nuclear transformation. Formation of crystals of foreign proteins enables simple purification, and also the folded crystals (e.g., *Bacillus thuringiensis* (Bt) toxin protein) crystals improve the safety of the Bt transgenic plants. Absence of the insecticidal protein in transgenic pollen eliminates toxicity to non-target insects via pollen. Expression of cry2Aa2 operon in chloroplasts provides a model system for hyper-expression of foreign proteins in a folded configuration enhancing their stability and facilitating single step purification. The metal resistant plants generated by above mentioned methods effectively harvest precious and semi-precious metals and trap them in their plant tissues. 100 fold greater amounts of insecticidal protein can be found in plants co-expressing the chaperon protein versus plants having only the gene encoding the insecticidal protein.

Dwg.0/14

L210 ANSWER 11 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 2001-147325 [15] WPIDS  
 DOC. NO. CPI: C2001-043631  
 TITLE: Recombinant protein derived from ticks that is capable of inhibiting human mast cell tryptase activity, useful for treating and preventing inflammation in humans or animals, and for the depletion or removal of tryptase from a food product.  
 DERWENT CLASS: B04 D16  
 INVENTOR(S): NUTTALL, P A; PAESEN, G C  
 PATENT ASSIGNEE(S): (EVOL-N) EVOLUTEC LTD  
 COUNTRY COUNT: 95  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001005823	A2	20010125	(200115)*	EN	32
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000060040	A	20010205	(200128)		
BR 2000012589	A	20020409	(200232)		
EP 1196579	A2	20020417	(200233)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001005823	A2	WO 2000-GB2791	20000719
AU 2000060040	A	AU 2000-60040	20000719
BR 2000012589	A	BR 2000-12589	20000719
		WO 2000-GB2791	20000719
EP 1196579	A2	EP 2000-946166	20000719
		WO 2000-GB2791	20000719

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000060040	A Based on	WO 200105823
BR 2000012589	A Based on	WO 200105823
EP 1196579	A2 Based on	WO 200105823

PRIORITY APPLN. INFO: GB 1999-16913 19990719

AB WO 200105823 A UPAB: 20010317

NOVELTY - A recombinant protein (I), its active fragment or functional equivalent, derived from a blood-feeding arthropod ectoparasite, preferably ticks, that is capable of inhibiting the activity of a human mast cell tryptase, is new.

DETAILED DESCRIPTION - A recombinant protein (I), its active fragment or functional equivalent, derived from a blood-feeding arthropod ectoparasite, preferably ticks, that is capable of inhibiting the activity of a human mast cell tryptase, is new.

(I) exhibits significant sequence **homology** with the tick-derived protease inhibitor protein (TdPI; a 118 amino acid sequence (S1) as defined in the specification), its active fragment or its functional equivalent.

INDEPENDENT CLAIMS are also included for the following:

- (1) a vaccine composition (VC) comprising (I)
- (2) formulating VC, by bringing (I), its fragment or functional equivalent into association with a pharmaceutically acceptable carrier;
- (3) a nucleic acid molecule (II) encoding (I);
- (4) a nucleic acid molecule (IIa) having the 490 **nucleotide sequence** defined in the specification which **hybridizes** with (II) under stringent **hybridization** conditions, or which encodes (I);
- (5) a viral vector (III) comprising (II) or (IIa);
- (6) a host cell (IV) transformed or transfected with (III);
- (7) a transgenic animal (V) transformed by (II) or (IIa);
- (8) preparing (I) by culturing (IV); and
- (9) a method for vaccinating a mammal against a disease, or for treating a mammal suffering from a disease, comprising administering (I), its fragment or functional equivalent.

ACTIVITY - Antiinflammatory; antiasthmatic; antipsoriatic; antirheumatoid; antiarthritic; antiallergic; cytostatic.

MECHANISM OF ACTION - Inhibitor of tryptase, preferably human mast cell tryptase; vaccine (claimed); gene therapy.

No supporting biological data given.

USE - (I) is useful as a pharmaceutical and in the manufacture of a medicament for treating inflammation in **humans** and animals. (I) is useful for treating and preventing inflammation in **humans** or animals. One or more epitopes of (I) can be used in the development of vaccines that target proteins that exhibit significant sequence **homology** with TdPI. (I) is useful for vaccinating a **mammal** against a disease. Bovine colostrum **trypsin inhibitor**,

rat tissue factor pathway inhibitor (TFPI-2), Kunitz domain of tick anticoagulant peptide TAP or the two domains in ornithodorin, are useful as a tryptase inhibitor.

(I) is useful in the detection or quantification of tryptase, for the depletion or removal of tryptase from a food product or from a cell culture, as an anti-tryptase agent or as an antiinflammatory drug (all claimed).

(I) is useful for treating asthma, psoriasis, interstitial lung disease, rheumatoid arthritis, gingivitis, peridontitis, allergic reactions, cancer and any other tryptase-mediated condition. (I) is useful as an immunogen, and as a tool in the study of inflammation, inflammation-related processes, or other physiological processes involving tryptase. VC is useful for vaccinating against a broad range of arthropod and/or helminth genera.

Dwg.0/6

L210 ANSWER 12 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:812153 CAPLUS

DOCUMENT NUMBER: 136:65865

TITLE: Deamidation of human proteins

AUTHOR(S): Robinson, N. E.; Robinson, A. B.

CORPORATE SOURCE: Division of Chemistry and Chemical Engineering,  
California Institute of Technology, Pasadena, CA,  
91125, USA

SOURCE: Proceedings of the National Academy of Sciences of the  
United States of America (2001), 98(22), 12409-12413  
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Deamidation of asparaginyl and glutaminyl residues causes time-dependent changes in charge and conformation of peptides and proteins. Quant. and exptl. verified predictive calcns. of the deamidation rates of 1,371 asparaginyl residues in a representative collection of 126 human proteins have been performed. These rates suggest that deamidation is a biol. relevant phenomenon in a remarkably large percentage of human proteins.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L210 ANSWER 13 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:520875 CAPLUS

DOCUMENT NUMBER: 136:52537

TITLE: Interferon-.gamma. in healthy subjects: selective modulation of inflammatory mediators

AUTHOR(S): De Metz, J.; Hack, C. E.; Romijn, J. A.; Levi, M.;  
Out, T. A.; Ten Berge, I. J. M.; Sauerwein, H. P.

CORPORATE SOURCE: Academic Medical Centre, University of Amsterdam,  
Amsterdam, 1100 DE, Neth.

SOURCE: European Journal of Clinical Investigation (2001),  
31(6), 536-543

CODEN: EJCIB8; ISSN: 0014-2972

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It is suggested that interferon-.gamma. (IFN-.gamma.), like other cytokines, is a mediator in the host inflammatory response, which could be of importance in the pathophysiol. of sepsis. The role of IFN-.gamma. in human host inflammatory responses, however, has not been studied. In a placebo-controlled trial we studied the acute effects of IFN-.gamma. administration on host inflammatory mediators in healthy men: i.e. the

cytokine/chemokine cascade system, acute-phase proteins, activation markers of the innate cellular immunity and coagulation/fibrinolysis parameters. IFN- $\gamma$  increased plasma levels of interleukin-6 (IL-6), IL-8 and IFN- $\gamma$ -inducible protein-10 (IP-10), but did not affect plasma levels of other cytokines (IL-4, IL-10, tumor necrosis factor- $\alpha$ , IL-12p40/p70). Plasma concns. of C-reactive protein and secretory phospholipase A2 both increased. Plasma levels of the leukocyte activation marker elastase- $\alpha$ 1-antitrypsin complexes increased after IFN- $\gamma$  administration, IFN- $\gamma$  increased the percentage of high-affinity Fc $\gamma$ -receptor (Fc $\gamma$ RI) -pos. neutrophils, but did not affect the mean fluorescence intensity of Fc $\gamma$ RI on neutrophils. Procoagulant and profibrinolytic effects of IFN- $\gamma$  were evidenced by increased plasma levels of prothrombin fragment F1 + F2, tissue-plasminogen activator and plasmin- $\alpha$ 2-antiplasmin complexes. Thus, IFN- $\gamma$  selectively affects host inflammatory mediators in humans.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L210 ANSWER 14 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:133848 CAPLUS

DOCUMENT NUMBER: 132:190514

TITLE: Human proteases and associated proteins and cDNAs and their uses in drug screening and therapy

INVENTOR(S): Bandman, Olga; Hillman, Jennifer L.; Baughn, Mariah R.; Azimzai, Yalda; Guegler, Karl J.; Corley, Neil C.; Yue, Henry; Tang, Y. Tom; Reddy, Roopa; Patterson, Chandra; Au-young, Janice; Shih, Leo L.; Lu, Dyung Aina M.

PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 114 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000009709	A2	20000224	WO 1999-US17818	19990806
WO 2000009709	A3	20000908		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9953403	A1	20000306	AU 1999-53403	19990806
EP 1104473	A2	20010606	EP 1999-939042	19990806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:

US 1998-96114P P 19980810

US 1999-119768P P 19990211

WO 1999-US17818 W 19990806

AB The invention provides human proteases and assocd. proteins (PPRGs) and polynucleotides which identify and encode PPRG. The invention also provides expression vectors, host cells, antibodies, agonists, and

antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders assocd. with expression of PPRG.

L210 ANSWER 15 OF 67 USPATFULL

ACCESSION NUMBER: 2000:138080 USPATFULL  
 TITLE: Recombinant methods for production of serine protease inhibitors and DNA sequences useful for same  
 INVENTOR(S): Bandyopadhyay, Pradip K., Boulder, CO, United States  
 Eisenberg, Stephen P., Boulder, CO, United States  
 Stetler, Gary L., Lafayette, CO, United States  
 Thompson, Robert C., Boulder, CO, United States  
 PATENT ASSIGNEE(S): Amgen Boulder Inc., Boulder, CO, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6132990		20001017
APPLICATION INFO.:	US 1991-712354		19910607 (7)
RELATED APPLN. INFO.:	Division of Ser. No. US 1989-293042, filed on 3 Jan 1989, now abandoned which is a continuation-in-part of Ser. No. US 1987-82962, filed on 4 Aug 1987, now abandoned And a continuation-in-part of Ser. No. US 1987-31846, filed on 30 Mar 1987, now abandoned And a continuation-in-part of Ser. No. US 1986-890526, filed on 29 Jul 1986, now abandoned which is a continuation-in-part of Ser. No. US 1985-803471, filed on 2 Dec 1985, now abandoned which is a continuation-in-part of Ser. No. US 1984-678822, filed on 6 Dec 1984, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Wax, Robert A.		
ASSISTANT EXAMINER:	Moore, William W.		
LEGAL REPRESENTATIVE:	Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.		
NUMBER OF CLAIMS:	83		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 7 Drawing Page(s)		
LINE COUNT:	3196		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			

AB A synthetic DNA **sequence** and its genetic equivalents are disclosed which **sequences** are capable, when used in a recombinant DNA method, of directing production of a serine protease inhibitor protein. Recombinant DNA methods for the production of serine **protease inhibitor** proteins are also disclosed. These methods incorporate either the synthetic DNA **sequence** of the present invention or natural DNA **sequences** isolated from **human** cDNA or genomic libraries.

In addition, a single polypeptide chain protein is disclosed which is capable of inhibiting chymotrypsin and elastase but not **trypsin**. In one embodiment, this protein is a shortened form (single domain) of the protein produced by the method described herein.

L210 ANSWER 16 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2000-182719 [16] WPIDS  
 DOC. NO. CPI: C2000-057316  
 TITLE: Novel screen comprising a pool of vectors with randomly modified **nucleotide sequences**, useful for identifying modulators of enzyme activity useful for selecting antibiotic agents.

DERWENT CLASS: B04 D13 D15 D16  
 INVENTOR(S): HALKIER, T; JENSEN, A; JESPERSEN, L  
 PATENT ASSIGNEE(S): (MEBI-N) M & E BIOTECH AS; (PHAR-N) PHARMEXA AS; (INOX-N) INOXELL AS  
 COUNTRY COUNT: 87  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000005406	A1	20000203	(200016)	* EN	136
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9948985	A	20000214	(200029)		
EP 1098991	A1	20010516	(200128)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
NO 2001000300	A	20010319	(200129)		
CZ 2001000210	A3	20010613	(200138)		
HU 2001002457	A2	20011029	(200175)		
SK 2001000069	A3	20011203	(200203)		
ZA 2001000195	A	20020327	(200230)		188
KR 2001103560	A	20011123	(200232)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000005406	A1	WO 1999-DK408	19990716
AU 9948985	A	AU 1999-48985	19990716
EP 1098991	A1	EP 1999-932689	19990716
		WO 1999-DK408	19990716
NO 2001000300	A	WO 1999-DK408	19990716
		NO 2001-300	20010118
CZ 2001000210	A3	WO 1999-DK408	19990716
		CZ 2001-210	19990716
HU 2001002457	A2	WO 1999-DK408	19990716
		HU 2001-2457	19990716
SK 2001000069	A3	WO 1999-DK408	19990716
		SK 2001-69	19990716
ZA 2001000195	A	ZA 2001-195	20010108
KR 2001103560	A	KR 2001-700871	20010119

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9948985	A Based on	WO 200005406
EP 1098991	A1 Based on	WO 200005406
CZ 2001000210	A3 Based on	WO 200005406
HU 2001002457	A2 Based on	WO 200005406
SK 2001000069	A3 Based on	WO 200005406

PRIORITY APPLN. INFO: US 1998-94868P 19980729; DK 1998-956  
 19980720

AB WO 200005406 A UPAB: 20000330  
 NOVELTY - Cell screen (I) comprising using a pool of expression vectors,

each with one member from a library of randomly modified **nucleotide sequence (NS)** encoding a scaffold portion of a parent peptide or RNA.

**DETAILED DESCRIPTION** - The screen (I) identifies an in vivo modulator of a target enzyme by preparing a pool of expression vectors, transforming a population of substantially identical cells harboring the enzyme, culturing the cells and isolating transformed cells where activity of the enzyme is modulated. The modulator is identified by determining a randomly modified vector NS and/or by determining the amino acid (aa) or **RNA sequence** of the expression product encoded by NS.

**INDEPENDENT CLAIMS** are also included for the following:

- (1) preparation of replicable vector;
- (2) cells transformed by the vector of (1);
- (3) producing an enzyme modulator comprising:
  - (a) growing a cell as in (2); and
  - (b) harvesting the expression product; or
  - (c) identifying the modulator according to (I); and
  - (d) synthesizing the modulator; and
- (4) isolating and/or identifying a target biomolecule (M1) using the modulator as an affinity ligand in an affinity purification step, or as a probe against a **cDNA** library derived from the cells harboring the enzyme or as bait in a two- or three-hybrid system.

**USE** - The screen is used for identification of modulators which in turn are used in selecting a chemical compound, a drug candidate in drug development (claimed). The compound is utilized for preparing a medicinal product (claimed). Modulators are further used for developing a medicinal product by serving as an interaction probe for identification of putative drug candidates in drug discovery phase (claimed) and thus antibiotic and antifungal agents are identified. Modulators are also used for identifying biomolecules which can be used for improving an industrial fermentation process.

**DESCRIPTION OF DRAWING(S)** - The diagram shows a schematic representation of pCMVbipep/CI-2A with the functional cis-elements found in pCMVbipep indicated.  
Dwg.1/7

L210 ANSWER 17 OF 67 USPATFULL

ACCESSION NUMBER: 1999:155509 USPATFULL  
 TITLE: Kallikrein-inhibiting "Kunitz Domain" proteins and analogues thereof  
 INVENTOR(S): Markland, Willaim, Milford, MA, United States  
 Ladner, Robert Charles, Ijamsville, MD, United States  
 PATENT ASSIGNEE(S): Dyax Corp., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5994125		19991130
APPLICATION INFO.:	US 1998-136012		19980817 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1996-676125, filed on 25 Sep 1996, now patented, Pat. No. US 5795685 which is a continuation-in-part of Ser. No. US 1994-208264, filed on 10 Mar 1994 which is a continuation-in-part of Ser. No. US 1994-179964, filed on 11 Jan 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Degen, Nancy		
LEGAL REPRESENTATIVE:	Yankwich, Leon R., Zwicker, Kenneth P.		
NUMBER OF CLAIMS:	7		
EXEMPLARY CLAIM:	1		



LINE COUNT: 2594

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Proteins are disclosed that are **homologous** to bovine pancreatic **trypsin inhibitor** (BPTI) Kunitz domains, and especially proteins that are **homologous** to lipoprotein-associated coagulation inhibitor (LACI) Kunitz domains, which inhibit one or more plasma and/or tissue kallikreins, and uses of such proteins in therapeutic and diagnostic methods also are disclosed. In particular, Kunitz domains derived from Kunitz domains of **human** origin and especially to the first Kunitz domain of LACI are disclosed.

L210 ANSWER 18 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 2000-072182 [06] WPIDS  
 DOC. NO. CPI: C2000-020551  
 TITLE: New recombinant nucleic acid, with reduced GC content, encoding the serine protease ASP05, used for treating disorders involving insulin-like growth factor, e.g. cancer.  
 DERWENT CLASS: B04 C03 D16  
 INVENTOR(S): HOU, J; SMEEKENS, S P  
 PATENT ASSIGNEE(S): (AXYS-N) AXYS PHARM INC  
 COUNTRY COUNT: 84  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9955885	A2	19991104	(200006)*	EN	70
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL					
OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD					
GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV					
MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT					
UA UG UZ VN YU ZW					
AU 9936694	A	19991116	(200015)		
EP 1073755	A2	20010207	(200109)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT					
RO SE SI					
KR 2001043127	A	20010525	(200168)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9955885	A2	WO 1999-US9224	19990428
AU 9936694	A	AU 1999-36694	19990428
EP 1073755	A2	EP 1999-918882	19990428
		WO 1999-US9224	19990428
KR 2001043127	A	WO 1999-US9224	19990428
		KR 2000-712020	20001028

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9936694	A Based on	WO 9955885
EP 1073755	A2 Based on	WO 9955885

PRIORITY APPLN. INFO: US 1999-300621 19990427; US 1998-83321P  
 19980428

AB WO 9955885 A UPAB: 20011113

NOVELTY - Recombinant nucleic acid (I) has at least a 10% reduction in GC content compared with the sequence of wild-type nucleic acid (Ia) encoding serine protease ASP05.

DETAILED DESCRIPTION - (I) **hybridizes**, under highly stringent conditions, to nucleotides (nt) 481-1113 of a 1443 bp sequence (S1) (given in the specification), or its complement, and has at least a 10% reduction in GC content compared with the sequence of wild-type nucleic acid (Ia) encoding serine protease ASP05.

INDEPENDENT CLAIMS are also included for the following:

- (a) recombinant nucleic acid encoding amino acids (aa) 30-104 of a 480 aa sequence (S2) (given in the specification);
- (b) vector containing (I);
- (c) host cell containing (I) or this vector;
- (d) recombinant production of ASP05 protein (II) by culturing these cells;
- (e) enzymatically active (II) containing aa 161-371 or 1-480 of (S2);
- (f) any (II) encoded by (I);
- (g) chimeric molecule (IIa) containing the catalytic domain of ASP05 fused to a heterologous sequence;
- (h) antibodies (Ab) specific for (II);
- (i) selective cleavage of insulin-like growth factor (IGF) binding protein (IGFBP) by treatment with (IIa) containing aa 161-371 of (S2);
- (j) screening for agents (A) that modulate activity of (II), or any serine protease that can cleave IGFBP selectively;
- (k) modulating cleavage of IGF-BP by administering an exogenous modulator of ASP05; and
- (l) diagnosing an IGF-related condition by detecting abnormal activity of ASP05, relative to a control.

ACTIVITY - Anticancer; antiproliferative; anti-angiogenic.

MECHANISM OF ACTION - ASP05 specifically cleaves IGFBP.

USE - (I) is used to produce recombinant ASP05 proteins (II), particularly in enzymatically active form or fragments, and these are used for selective cleavage of insulin-like growth factor binding protein (IGFBP). (II) can also be used:

- (1) to raise or purify specific antibodies (Ab);
  - (2) to identify modulators (A) of ASP05 (or other serine proteases with similar activity).
- (A), e.g. antisense sequences, antibodies or peptides, are used to reduce or eliminate biological activity of ASP05 proteins, particularly therapeutically, e.g. in cases of cancer; other cell proliferation conditions (restenosis, angiogenesis, neovascularization of the eye etc.); bone metabolic diseases (osteoporosis or osteoarthritis) and diseases of muscle, brain, ovary, uterus and placenta, in human or veterinary medicine. Ab are used therapeutically or for purification of recombinant (II). Determining abnormal levels of ASP05 in tissues is indicative of (risk of) an IGF-related disorder.

ADVANTAGE - (I) is easier to express in transformed cells than the wild-type ASP05 sequence, which has a GC-rich N-terminus.  
Dwg.0/8

L210 ANSWER 19 OF 67 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1999-371118 [31] WPIDS  
CROSS REFERENCE: 1999-229499 [19]; 1999-229532 [19]; 1999-229533 [19];  
1999-254381 [19]; 1999-254713 [21]; 1999-302739 [24];  
1999-326705 [25]; 1999-337420 [25]; 1999-347718 [29];  
1999-404743 [29]; 1999-430385 [35]; 1999-551358 [46];  
1999-580306 [47]; 1999-620728 [53]; 2000-038358 [03];  
2000-062031 [04]; 2000-072883 [05]; 2000-116314 [09];  
2000-237871 [20]; 2000-271386 [23]; 2000-271431 [23];

2000-271434 [23]; 2000-271435 [23]; 2000-292842 [24];  
 2000-317943 [27]; 2000-412154 [35]; 2000-412324 [35];  
 2000-412325 [35]; 2000-431586 [37]; 2000-442668 [38];  
 2000-452188 [38]; 2000-572269 [52]; 2000-572270 [52];  
 2000-572271 [52]; 2000-587437 [52]; 2000-594320 [52];  
 2000-594321 [52]; 2000-611443 [52]; 2000-611444 [52];  
 2000-628263 [55]; 2000-638138 [52]; 2000-638201 [53];  
 2000-679484 [59]; 2001-016509 [02]; 2001-025022 [66];  
 2001-025251 [02]; 2001-025253 [02]; 2001-032160 [02];  
 2001-050025 [04]; 2001-050091 [05]; 2001-070561 [59];  
 2001-071075 [04]; 2001-071078 [04]; 2001-071395 [06];  
 2001-081051 [09]; 2001-090793 [52]; 2001-091968 [10];  
 2001-103149 [11]; 2001-183260 [18]; 2001-226690 [20];  
 2001-226823 [23]; 2001-235264 [23]; 2001-381383 [39];  
 2001-381384 [39]; 2001-408281 [39]; 2001-451708 [43];  
 2001-541567 [53]; 2001-602746 [62]; 2001-625876 [60];  
 2002-075461 [03]; 2002-090516 [09]; 2002-130120 [14];  
 2002-130151 [22]; 2002-130882 [09]; 2002-171999 [22];  
 2002-172001 [22]; 2002-205567 [49]; 2002-256031 [46];  
 2002-280917 [30]; 2002-280928 [30]; 2002-280940 [30];  
 2002-292065 [30]

DOC. NO. CPI: C1999-109584

TITLE: Nucleic acids encoding PRO secreted and transmembrane proteins.

DERWENT CLASS: B04 D16 S03

INVENTOR(S): BAKER, K P; CHEN, J; GODDARD, A; GURNEY, A L; WOOD, W I; YUAN, J; GURNEY, A

PATENT ASSIGNEE(S): (GETH) GENENTECH INC; (LUCE) LUCENT TECHNOLOGIES INC; (BAKE-I) BAKER K P; (CHEN-I) CHEN J; (GODD-I) GODDARD A; (GURN-I) GURNEY A L; (WOOD-I) WOOD W I; (YUAN-I) YUAN J

COUNTRY COUNT: 85

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9928462	A2	19990610	(199931)*	EN	123
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9916029	A	19990616	(199945)		
ZA 9811071	A	19991027	(199951)		123
AU 9922122	A	19990726	(199952)		
JP 11355431	A	19991224	(200011)		11
CN 1240321	A	20000105	(200021)		
EP 1037979	A2	20000927	(200048)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 736506	B	20010726	(200149)		
KR 2001032719	A	20010425	(200164)		
MX 2000005354	A1	20010401	(200171)		
JP 2002505850	W	20020226	(200219)		202
EP 1191101	A2	20020327	(200229)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9928462	A2	WO 1998-US25108	19981201
AU 9916029	A	AU 1999-16029	19981201
ZA 9811071	A	ZA 1998-11071	19981203
AU 9922122	A	AU 1999-22122	19990105
JP 11355431	A	JP 1999-130879	19990512
CN 1240321	A	CN 1999-106448	19990511
EP 1037979	A2	EP 1998-960440	19981201
		WO 1998-US25108	19981201
AU 736506	B	AU 1999-16029	19981201
KR 2001032719	A	WO 1998-US25108	19981201
		KR 2000-706008	20000602
MX 2000005354	A1	MX 2000-5354	20000531
JP 2002505850	W	WO 1998-US25108	19981201
		JP 2000-523338	19981201
EP 1191101	A2 Div ex	EP 1998-960440	19981201
		EP 2001-126188	19981201

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9916029	A Based on	WO 9928462
AU 9922122	A Based on	WO 9935170
EP 1037979	A2 Based on	WO 9928462
AU 736506	B Previous Publ.	AU 9916029
	Based on	WO 9928462
JP 2002505850	W Based on	WO 9928462
EP 1191101	A2 Div ex	EP 1037979

PRIORITY APPLN. INFO: US 1998-75945P 19980225; US 1997-67411P 19971203; US 1997-69278P 19971211; US 1997-69334P 19971211; US 1997-69335P 19971211; US 1997-69425P 19971212; US 1997-69694P 19971216; US 1997-69696P 19971216; US 1997-69702P 19971216; US 1997-69870P 19971217; US 1997-69873P 19971217; US 1997-68017P 19971218; US 1998-70440P 19980105; US 1998-74086P 19980209; US 1998-74092P 19980209; US 1998-83500P 19980429; US 1998-86414P 19980522; US 1998-88742P 19980610; US 1998-107783P 19981110; US 1998-109304P 19981120; US 1998-75945 19980512

AB WO 9928462 A UPAB: 20020524  
NOVELTY - Nucleic acids encoding PRO secreted and transmembrane proteins used therapeutically are new.

DETAILED DESCRIPTION - A novel nucleic acid is at least 80% identical to a sequence encoding a PRO polypeptide having a 379, 954, 737, 433, 446, 422, 300, 243, 455, 694, 440, 598, 250, 281, 431 or 235 amino acid sequence (all given in the specification).

INDEPENDENT CLAIMS are also included for the following:

- (1) a vector comprising a nucleic acid as above;
- (2) a host cell comprising a vector as in (1);
- (3) production of a PRO polypeptide as above; a PRO polypeptide at least 80% identical to a sequence as described above;
- (4) a chimeric molecule comprising a PRO polypeptide as above fused to a heterologous amino acid sequence; and
- (5) an antibody which specifically binds to a PRO polypeptide as

above.

ACTIVITY - Cytostatic; Anti-inflammatory; Anti-proliferative; Immunosuppressive.

MECHANISM OF ACTION - None given.

USE - The proteins and polynucleotides can be used in therapy, identification of **homologues**, raising antibodies and design of probes and primers. They can be used in a range of diseases related to proteins that they have **homology** with, e.g. a PRO protein having **homology** to complement proteins may be used in inflammatory responses.

ADVANTAGE - None given.

Dwg.0/39

L210 ANSWER 20 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999335882 EMBASE

TITLE: Inactivation of proprotein convertase, PACE4, by .alpha.1-antitrypsin portland (.alpha.1-PDX), a blocker of proteolytic activation of bone morphogenetic protein during embryogenesis: Evidence that PACE4 is able to form an SDS-stable acyl intermediate with .alpha.1-PDX.

AUTHOR: Tsuji A.; Hashimoto E.; Ikoma T.; Taniguchi T.; Mori K.; Nagahama M.; Matsuda Y.

CORPORATE SOURCE: Y. Matsuda, Dept. Biological Science Technology, Faculty of Engineering, The University of Tokushima, 2-1 Minamijosanjima, Tokushima 770 8506, Japan. matsuda@bio.tokushima-u.ac.jp

SOURCE: Journal of Biochemistry, (1999) 126/3 (591-603). Refs: 51

ISSN: 0021-924X CODEN: JOBIAO

COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 021 Developmental Biology and Teratology  
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB PACE4 (SPC4), a member of the subtilisin-like proprotein convertase (SPC) family of proteases that cleave at paired basic amino acids, exhibits a dynamic expression pattern during embryogenesis and colocalizes with bone morphogenetic proteins (BMPs). Recently Cui et al. reported that the ectopic expression of .alpha.1-antitrypsin variant Portland (.alpha.1-PDX), an engineered serpin that contains the minimal SPC consensus motif in its reactive loop, blocks the proteolytic activation of BMP4, leading to abnormal embryogenic development TGF.beta.-related factors such as BMPs are synthesized as inactive precursors and activated by limited proteolysis at multibasic amino acids. Therefore, an .alpha.1-PDX-inhibitable protease is thought to participate in BMP activation. However, conflicting properties, including sensitivity to .alpha.1-PDX, have been reported for PACE4. In this study, we examined whether .alpha.1-PDX is responsible for the inhibition of PACE4 by measuring the protease/inhibitor complex directly. Here we show that .alpha.1-PDX has the ability to form an SDS-stable acyl-intermediate (180 kDa) with PACE4 in vivo and in vitro. Further, we characterized the PACE4 secreted into the culture medium from Cos-1 cells by a specific immunological assay. An .alpha.1-PDX-insensitive and decanoyl-RVKR-chloromethylketone-sensitive 60-kDa protease(s) is greatly activated in conditioned medium by PACE4 overexpression, suggesting that the activation of an unknown protease(s) other than PACE4 is the cause of the variation in the properties of PACE4. PACE4 is a Ca<sup>2+</sup>-dependent protease with an optimal Ca<sup>2+</sup> requirement of 2 mM, and shows its highest activity at weakly basic pH. PACE4 activity is completely inhibited by EDTA and EGTA, but not

by leupeptin. These results show that PACE4 activity can be inhibited by (.alpha.1-PDX as well as furin (SPC1) and suggest that the inhibition of PACE4-mediated activation of factors such as BMPs by .alpha.1-PDX causes abnormal embryogenic development.

L210 ANSWER 21 OF 67 USPATFULL

ACCESSION NUMBER: 1998:98889 USPATFULL  
 TITLE: Kallikrein-inhibiting "kunitz domain" proteins and analogues thereof  
 INVENTOR(S): Markland, Willaim, Milford, MA, United States  
 Ladner, Robert Charles, Ijamsville, MD, United States  
 PATENT ASSIGNEE(S): Dyax Corp., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5795865		19980818
	WO 9521601		19950817
APPLICATION INFO.:	US 1996-676125		19960925 (8)
	WO 1995-US299		19950111
			19960925 PCT 371 date
			19960925 PCT 102(e) date
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-208264, filed on 10 Mar 1994, now abandoned And a continuation-in-part of Ser. No. US 1994-179964, filed on 11 Jan 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Degen, Nancy		
LEGAL REPRESENTATIVE:	Yankwich, Leon R., Cooper, Iver P.		
NUMBER OF CLAIMS:	13		
EXEMPLARY CLAIM:	1		
LINE COUNT:	2161		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Proteins are disclosed that are **homologous** to bovine pancreatic **trypsin inhibitor** (BPTI) Kunitz domains, and especially proteins that are **homologous** to lipoprotein-associated coagulation inhibitor (LACI) Kunitz domains, which inhibit one or more plasma and/or tissue kallikreins, and uses of such proteins in therapeutic and diagnostic methods also are disclosed. In particular, Kunitz domains derived from Kunitz domains of **human** origin and especially to the first Kunitz domain of LACI are disclosed.

L210 ANSWER 22 OF 67 USPATFULL

ACCESSION NUMBER: 1998:95406 USPATFULL  
 TITLE: Isolated DNA encoding novel protease inhibitory polypeptide  
 INVENTOR(S): Morishita, Hideaki, Tokyo, Japan  
 Kanamori, Toshinori, Tokyo, Japan  
 Nobuhara, Masahiro, Tokyo, Japan  
 PATENT ASSIGNEE(S): Mochida Pharmaceutical Co., Ltd., Tokyo, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5792629		19980811
APPLICATION INFO.:	US 1994-293150		19940819 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1991-791213, filed on 13 Nov 1991, now patented, Pat. No. US 5409895		

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1990-306745	19901113
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Wax, Robert A.	
ASSISTANT EXAMINER:	Grimes, Eric	
LEGAL REPRESENTATIVE:	Burns, Doane, Swecker & Mathis, LLP	
NUMBER OF CLAIMS:	29	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	50 Drawing Figure(s); 34 Drawing Page(s)	
LINE COUNT:	5022	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel polypeptide which comprises an amino acid **sequence** that constitutes a portion of urinary **trypsin** inhibitor (UTI) and which has no antigenicity against **human** and high activity to **inhibit** various **proteases**, as well as other novel polypeptides having excellent activities to **inhibit** various **proteases** obtained by mutation of the former novel polypeptide. This invention also provides novel enzyme inhibition processes, drug compositions and treating methods making use of the novel polypeptide, DNA fragments containing nucleotide **sequences** which encode the novel polypeptides, vectors containing the DNA fragments and transformants transformed with the DNA fragments or the vectors, as well as processes for the production of the novel polypeptides.

L210 ANSWER 23 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 1999-070328 [06] WPIDS  
 DOC. NO. CPI: C1999-020862  
 TITLE: Production of heterologous polypeptide containing many disulphide bonds in bacteria - that also express a disulphide isomerase to ensure proper folding and increased yield of biologically active product, e.g. tissue plasminogen activator or pancreatic trypsin inhibitor.  
 DERWENT CLASS: B04 D16  
 INVENTOR(S): BESSETTE, P; GEORGIOU, G; QIU, J; SWARTZ, J R; OIU, J; SWARTZ, J  
 PATENT ASSIGNEE(S): (TEXA) UNIV TEXAS SYSTEM; (GETH) GENENTECH INC  
 COUNTRY COUNT: 83  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9856930	A2	19981217	(199906)*	EN	97
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL					
OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE					
GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG					
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG					
US UZ VN YU ZW					
AU 9881404	A	19981230	(199920)		
EP 1002111	A2	20000524	(200030)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6083715	A	20000704	(200036)		
JP 2002504826	W	20020212	(200215)		106
AU 743030	B	20020117	(200219)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9856930	A2	WO 1998-US12004	19980609
AU 9881404	A	AU 1998-81404	19980609
EP 1002111	A2	EP 1998-931228	19980609
		WO 1998-US12004	19980609
US 6083715	A	US 1997-871483	19970609
JP 2002504826	W	WO 1998-US12004	19980609
		JP 1999-503144	19980609
AU 743030	B	AU 1998-81404	19980609

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9881404	A Based on	WO 9856930
EP 1002111	A2 Based on	WO 9856930
JP 2002504826	W Based on	WO 9856930
AU 743030	B Previous Publ. Based on	AU 9881404 WO 9856930

PRIORITY APPLN. INFO: US 1997-871483 19970609

AB WO 9856930 A UPAB: 19990210

Production of a heterologous polypeptide (I) comprises culturing bacteria that contain (i) nucleic acid (NA1) encoding a disulphide isomerase (DsbG) protein (II); (ii) nucleic acid (NA2) encoding (I); (iii) signal sequence for secretion of both (I) and (II) and (iv) separate inducible promoters for NA1 and 2. The cells are cultured such that (II) is expressed before (I), and such that (a) both (I) and (II) are secreted into the periplasm or (b) (I) is secreted into the culture medium. (I) is then recovered from periplasm or medium. Also new are (1) method for producing biologically active, soluble eukaryotic polypeptide (Ia) with four or more disulphide bridges by expressing, in bacteria, a DNA encoding DsbC or DsbG linked to a signal sequence, and a second DNA encoding (Ia), also linked to a signal sequence; (2) bacterial expression system that expresses DsbC or G protein and recombinant eukaryotic polypeptide (Ib) with four or more disulphide bonds; (3) recombinant vector containing first transcription unit encoding E. coli DsbC or G linked to a signal sequence and second such unit expressing **mammalian** tissue plasminogen activator (tPA) or pancreatic **trypsin inhibitor** (PTI); (4) active tPA or PTI linked to a bacterial export signal peptide; (5) soluble, recombinant **human** tPA, protein or peptide, isolated from the periplasm of a cell in biologically active form; (6) E. coli ATCC 98380; (7) polypeptide (III) containing at least 15 contiguous amino acids (aa) from a 268 aa sequence reproduced (the DsbG protein) and able to catalyse disulphide bond formation; (8) polynucleotide (IV) encoding a bacterial disulphide isomerase containing at least 40 contiguous nucleotides (nt) from a 46 nt sequence reproduced (or with a sequence that **hybridises** with this under stringent conditions); (9) production of recombinant tPA in bacteria by co-expression with a cysteine oxidoreductase that facilitates production of active tPA.

USE - The methods are particularly used to produce insulin-like growth factor (IGF), or its receptor, tPA and PTI, but more generally any (I) that contains numerous disulphide bonds (e.g. antibody fragments, enzymes, lymphokines, neurotrophins and many others disclosed).

ADVANTAGE - Co-expression with DsbG or C results in active, correctly folded (I), even where this contains many disulphide bridges. (I) are produced in much increased yield, without requiring addition of



glutathione or co-expression of the heat-shock transcription factor RpoH. Production of (I) in secreted form facilitates purification, i.e. no need to solubilise and refold material present in inclusion bodies, and results in a product of higher activity.  
Dwg.1B/11

L210 ANSWER 24 OF 67 MEDLINE  
ACCESSION NUMBER: 1998352217 MEDLINE  
DOCUMENT NUMBER: 98352217 PubMed ID: 9685498  
TITLE: Divergent expression of alpha1-protease inhibitor genes in mouse and human.  
AUTHOR: Tardiff J; Krauter K S  
CORPORATE SOURCE: Department of Molecular, Cellular and Developmental Biology, University of Colorado at Boulder, Campus Box 347, Boulder, CO 80309, USA.  
CONTRACT NUMBER: CA13330 (NCI)  
CA39553 (NCI)  
SOURCE: NUCLEIC ACIDS RESEARCH, (1998 Aug 15) 26 (16) 3794-9.  
Journal code: O8L; 0411011. ISSN: 0305-1048.  
PUB. COUNTRY: ENGLAND: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-M75716; GENBANK-M75717; GENBANK-M75718;  
GENBANK-M75720; GENBANK-M75721  
ENTRY MONTH: 199809  
ENTRY DATE: Entered STN: 19981006  
Last Updated on STN: 20000303  
Entered Medline: 19980922

AB The alpha1-protease inhibitor proteins of laboratory mice are homologous in sequence and function to human alpha1-antitrypsin and are encoded by a highly conserved multigene family comprised of five members. In humans, the inhibitor is expressed in liver and in macrophages and decreased expression or inhibitory activity is associated with a deficiency syndrome which can result in emphysema and liver disease in affected individuals. It has been proposed that macrophage expression may be an important component of the function of human alpha1-antitrypsin. Clearly, it is desirable to develop a mouse model of this deficiency syndrome, however, efforts to do this have been largely unsuccessful. In this paper, we report that aside from the issues of potentially redundant gene function, the mouse may not be a suitable animal for such studies, because there is no significant expression of murine alpha1-protease inhibitor in the macrophages of mice. This difference between the species appears to result from an absence of a functional macrophage-specific promoter in mice.

L210 ANSWER 25 OF 67 MEDLINE  
ACCESSION NUMBER: 97277372 MEDLINE  
DOCUMENT NUMBER: 97277372 PubMed ID: 9115294  
TITLE: Identification and cloning of human placental bikunin, a novel serine protease inhibitor containing two Kunitz domains.  
AUTHOR: Marlbor C W; Delaria K A; Davis G; Muller D K; Greve J M; Tamburini P P  
CORPORATE SOURCE: Institute of Bone and Joint Disease and Cancer, Bayer Corporation, West Haven, Connecticut 06516, USA.  
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 May 2) 272 (18) 12202-8.  
Journal code: HIV; 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: GENBANK-U78095  
 ENTRY MONTH: 199706  
 ENTRY DATE: Entered STN: 19970612  
 Last Updated on STN: 19970612  
 Entered Medline: 19970602

AB Interrogation of the public expressed sequence tag (EST) data base with the sequence of preproaprotinin identified ESTs encoding two potential new members of the Kunitz family of serine protease inhibitors. Through reiterative interrogation, an EST contig was obtained, the consensus sequence from which encoded both of the novel Kunitz domains in a single open reading frame. This consensus sequence was used to direct the isolation of a full-length cDNA clone from a placental library. The resulting cDNA sequence predicted a 252-residue protein containing a putative NH2-terminal signal peptide followed sequentially by each of the two Kunitz domains within a 170-residue ectodomain, a putative transmembrane domain, and a 31-residue hydrophilic COOH terminus. The gene for this putative novel protein was mapped by use of a radiation hybrid panel to chromosome 19q13, and Northern analysis showed that the corresponding mRNA was expressed at high levels in human placenta and pancreas and at lower levels in brain, lung, and kidney. An endogenous soluble form of this protein, which was designated as placental bikunin, was highly purified from human placenta by sequential kallikrein-Sepharose affinity, gel filtration, and C18 reverse-phase chromatography. The natural protein exhibited the same NH2 terminus as predicted from the cloned cDNA and inhibited trypsin, plasma kallikrein, and plasmin with IC50 values in the nanomolar range.

L210 ANSWER 26 OF 67 USPATFULL

ACCESSION NUMBER: 96:27176 USPATFULL  
 TITLE: Agent for treating or preventing AIDS using  
**human urine trypsin inhibitor**  
 INVENTOR(S): Hattori, Toshio, Kumamoto, Japan  
 Takatsuki, Kiyoshi, Kumamoto, Japan  
 Yuki, Yoshikazu, Kobe, Japan  
 PATENT ASSIGNEE(S): JCR Pharmaceuticals Co., Ltd., Hyogo, Japan (non-U.S.  
 corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5504065		19960402
APPLICATION INFO.:	US 1994-261746		19940617 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1993-158819, filed on 26 Nov 1993, now abandoned which is a continuation of Ser. No. US 1992-960199, filed on 9 Oct 1992, now abandoned which is a continuation of Ser. No. US 1992-831080, filed on 5 Feb 1992, now abandoned which is a continuation of Ser. No. US 1989-436830, filed on 15 Nov 1989, now abandoned		

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1988-302058	19881128
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Schain, Howard E.	
LEGAL REPRESENTATIVE:	Burgess, Ryan and Wayne	
NUMBER OF CLAIMS:	2	
EXEMPLARY CLAIM:	1	

NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT: 273

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Human urine trypsin inhibitor is provided as an agent for treating acquired immunodeficiency syndrome (AIDS), preventing the infection with AIDS or preventing the onset of AIDS after such infection. It can be administered intravenously for the treatment and externally for the prevention.

L210 ANSWER 27 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96187771 EMBASE

DOCUMENT NUMBER: 1996187771

TITLE: Isolation and characterization of the human inter-.alpha.-trypsin inhibitor family heavy chain-related protein (IHRP) gene (ITIHL1).

AUTHOR: Saguchi K.-I.; Tobe T.; Hashimoto K.; Nagasaki Y.; Oda E.; Nakano Y.; Miura N.-H.; Tomita M.

CORPORATE SOURCE: Dept. of Physiological Chemistry, School of Pharmaceutical Sciences, Showa University, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 242, Japan

SOURCE: Journal of Biochemistry, (1996) 119/5 (898-905).

ISSN: 0021-924X CODEN: JOBIAO

COUNTRY: Japan

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Inter-.alpha.-trypsin inhibitor (ITI) family heavy chain-related protein (IHRP) is a novel human glycoprotein that shows significant homology in amino acid sequence to proteins of the ITI family heavy chains from human plasma. Three overlapping clones that encode the human inter-.alpha.-trypsin inhibitor family heavy chain-related protein (IHRP) gene (ITIHL1) were isolated and characterized. The IHRP gene spans 15 kb and is composed of 24 exons from 27 to 207 bp in size with consensus splice sites. The gene codes for the precursor of IHRP, which is similar to inter-a-trypsin inhibitor (ITI) family heavy chains. Two major transcription initiation sites were identified in the 5'-flanking region. They contain putative promoter elements, but no typical TATA box. Some exons of this gene showed significant similarities to those of the ITI-H1 gene in nucleotide length and in intron phasing. The tissue-specific transcription of this gene may be due to the presence of binding sites for the hepatocyte nuclear factors LF-A1, HNF-5, NP-IL6, and C/EBP. This gene was found to be localized very close to another unknown gene related to EST (GenBank accession: R54643, R50663, R50563, H27139, and R54913).

L210 ANSWER 28 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96115912 EMBASE

DOCUMENT NUMBER: 1996115912

TITLE: CDNA cloning and primary structure of tryptase from bovine mast cells, and evidence for the expression of bovine pancreatic trypsin inhibitor mRNA in the same cells.

AUTHOR: Pallaoro M.; Gambacurta A.; Fiorucci I.; Mignogna G.; Barra D.; Ascoli F.

CORPORATE SOURCE: Dpt. Medic. Speriment./Sci. Biochim., Universita Tor Vergata, Via di Tor Vergata 135, I-00133 Roma, Italy

SOURCE: European Journal of Biochemistry, (1996) 237/1 (100-105).

ISSN: 0014-2956 CODEN: EJBICAI

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB A partial cDNA encoding bovine tryptase, an oligomeric serine proteinase previously isolated from bovine mast cells, was obtained by reverse transcription/polymerase chain reaction of mast cell mRNA, using combinations of primers designed on the basis of information obtained from partial sequencing of the purified protein. The complete amino acid sequence of bovine tryptase (245 residues) was deduced from a 711-bp nucleotide sequence and from Edman degradation of the protein. Bovine tryptase primary structure has an identity of about 75 % with tryptases from other species-and includes all the essential residues of the active-site regions; sequence data in the region of the putative substrate binding pocket suggest a rearrangement capable of maintaining the specificity of trypsin-like proteinases. From the same mast cell mRNA, cDNA encoding bovine trypsin protease inhibitor (BPTI) was obtained and amplified with specific primers, confirming the synthesis of BPTI in these cells. Results are consistent with previous data on the presence of BPTI and bovine tryptase in the same granules of bovine mast cells and with their interaction in vitro.

L210 ANSWER 29 OF 67 USPATFULL

ACCESSION NUMBER: 95:36370 USPATFULL  
 TITLE: Protease inhibitory polypeptides derived from urinary trypsin inhibitor and compositions thereof  
 INVENTOR(S): Morishita, Hideaki, Tokyo, Japan  
 Kanamori, Toshinori, Tokyo, Japan  
 Nobuhara, Masahiro, Tokyo, Japan  
 PATENT ASSIGNEE(S): Mochida Pharmaceutical Co., Ltd., Tokyo, Japan  
 (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5409895		19950425
APPLICATION INFO.:	US 1991-791213		19911113 (7)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1990-306745	19901113
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Wax, Robert A.	
ASSISTANT EXAMINER:	Grimes, Eric	
LEGAL REPRESENTATIVE:	Burns, Doane, Swecker & Mathis	
NUMBER OF CLAIMS:	10	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	50 Drawing Figure(s); 34 Drawing Page(s)	
LINE COUNT:	3694	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a novel polypeptide which comprises an amino acid **sequence** that constitutes a portion of urinary **trypsin** inhibitor (UTI) and which has no antigenicity against **human** and high activity to **inhibit** various **proteases**, as well as other novel polypeptides having excellent activities to **inhibit** various **proteases** obtained by mutation of the former novel polypeptide. This invention also provides novel enzyme inhibition processes, drug compositions and treating methods making use of the novel polypeptide, DNA fragments containing nucleotide **sequences** which encode the novel polypeptides, vectors containing the DNA fragments and transformants transformed with

the DNA fragments or the vectors, as well as processes for the production of the novel polypeptides.

L210 ANSWER 30 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 95078767 EMBASE

DOCUMENT NUMBER: 1995078767

TITLE: The three heavy-chain precursors for the inter-.alpha.-inhibitor family in mouse: New members of the multicopper oxidase protein group with differential transcription in liver and brain.

AUTHOR: Chan P.; Risler J.-L.; Raguenez G.; Salier J.-P.

CORPORATE SOURCE: INSERM U-78, BP 73,76233 Boisguillaume Cedex, France

SOURCE: Biochemical Journal, (1995) 306/2 (505-512).

ISSN: 0264-6021 CODEN: BIJOAK

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The inter-.alpha.-inhibitor (I.alpha.I) family is comprised of the plasma protease inhibitors I.alpha.I, inter-.alpha.-like inhibitor (I.alpha.LI), pre-.alpha.-inhibitor (P.alpha.I) and bikunin. I.alpha.I, I.alpha.LI and P.alpha.I are distinct assemblies of bikunin with one of three heavy (H) chains designated H1, H2 and H3. These H chains and bikunin are respectively encoded by a set of three H genes and an .alpha.1-microglobulin/bikunin precursor (AMBP) gene. All four gene products undergo maturation steps from precursor polypeptides. The full-length cDNAs for the H1-, H2- and H3-chain precursors were cloned from a mouse liver cDNA library and sequenced. Extensive searches of amino acid sequence similarities to other proteins in databanks revealed (i) a highly significant similarity of the C-terminal sequence in the three H-chain precursors to the multicopper-binding domain in the group of multicopper oxidase proteins and (ii) the presence of von Willebrand type-A domains in the mature H chains. Amino acid sequence comparisons between the three mouse H1-, H2- and H3-chain precursors and their human counterparts allowed us to appraise the timing and order of occurrence of the three H-chain genes from a shared ancestor during mammalian evolution. Owing to a multiple alignment of the six mouse and human nucleotide sequences for these H-chain precursors, a reverse transcriptase PCR assay with degenerate oligonucleotides was designed, allowing us to (i) present evidence that no mRNAs for further H genes exist in mouse liver and (ii) demonstrate a previously undescribed transcription of the H2- and H3-chain mRNAs in mouse brain, which contrasts with the expression of all four, H1, H2, H3 and AMBP, mRNAs in liver.

L210 ANSWER 31 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 95282561 EMBASE

DOCUMENT NUMBER: 1995282561

TITLE: Pancreatic secretory trypsin inhibitor gene is highly expressed in the liver of adult-onset type II citrullinemia.

AUTHOR: Kobayashi K.; Nakata M.; Terazono H.; Shinsato T.; Saheki T.

CORPORATE SOURCE: Department of Biochemistry, Faculty of Medicine, Kagoshima University, Sakuragaoka 8-35-1, Kagoshima 890, Japan

SOURCE: FEBS Letters, (1995) 372/1 (69-73).

ISSN: 0014-5793 CODEN: FEBLAL

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics  
029 Clinical Biochemistry  
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Deficiency of argininosuccinate synthetase (ASS) causes citrullinemia. Type II citrullinemia is found in most patients with adult-onset citrullinemia in Japan, and ASS is deficient specifically in the liver. Previous studies have shown that the decrease of hepatic ASS activity is caused by a decrease in enzyme protein with normal kinetic properties and that there are no apparent abnormalities in the amount, translational activity, and nucleotide sequence of hepatic ASS mRNA. Recent results of homozygosity testing indicate that the primary defect of type II citrullinemia is not within the ASS gene locus. In this present work, to understand the pathogenesis and pathophysiology of type II citrullinemia, we have characterized the alterations of gene expression in the liver of type II patients using the recently developed mRNA differential display method. Some cDNA bands expressed differently in type II citrullinemia patients and control were selected, cloned, and sequenced. Nucleotide sequence analysis and homology searching revealed an interesting clone which has 99% homology with the human pancreatic secretory trypsin inhibitor (hPSTI). Northern blot and RT-PCR analyses showed that the expression of hPSTI mRNA increased significantly in the liver of all type II patients tested. Furthermore, the concentration of hPSTI protein was found to be higher in the liver of type II citrullinemia than in control. These results suggest that hPSTI may be related to the primary defect of type II citrullinemia and may be useful as a diagnostic marker, although the detailed mechanism of the high expression of hPSTI mRNA in type II liver is not yet known.

L210 ANSWER 32 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 94235128 EMBASE

DOCUMENT NUMBER: 1994235128

TITLE: Translational enhancement of H-ferritin mRNA by interleukin-1.beta. acts through 5' leader sequences distinct from the iron responsive element.

AUTHOR: Rogers J.T.; Andriotakis J.L.; Lacroix L.; Durmowicz G.P.; Kasschau K.D.; Bridges K.R.

CORPORATE SOURCE: Division of Hematology-Oncology, Department of Medicine, Brigham and Women's Hospital, Boston, MA 02115, United States

SOURCE: Nucleic Acids Research, (1994) 22/13 (2678-2686).

ISSN: 0305-1048 CODEN: NARHAD

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics  
026 Immunology, Serology and Transplantation  
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Interleukin-1.beta. (II-1.beta.), a key cytokine in the acute phase response, elevates hepatic expression of both the heavy (H) and light (L) ferritin subunits without influencing the steady-state levels of either ferritin transcript. Transfection experiments with human hepatoma cells reveal that sequences within the 5' untranslated region (5'UTR) of H-ferritin mRNA confer translational regulation to chimaeric chloramphenicol acetyl transferase (CAT) mRNAs in response to II-1.beta. in the absence of marked changes in CAT mRNA levels. dependent translational enhancement is mediated by a distinct G + C rich RNA sequence within 70 nucleotides (nt) of the start codon. The upstream Iron

Responsive Element RNA stemloop does not confer increased expression to CAT mRNA in II-1.beta. stimulated hepatoma transfectants. A 38 nucleotide consensus sequence within the 5'UTRs of the mRNAs encoding the hepatic acute phase proteins .alpha.1-antitrypsin (.alpha.1AT), .alpha.1-acid glycoprotein (AGP) and haptoglobin is similar to sequences in the G+C rich H-ferritin mRNA translational regulatory element. Deletion of three nucleotides from this region of the 61 nt G + C rich element in the H-ferritin mRNA 5' leader eliminates II-1.beta. translational enhancement of the CAT reporter transcripts.

L210 ANSWER 33 OF 67 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 93064647 EMBASE

DOCUMENT NUMBER: 1993064647

TITLE: Organization and sequence of the gene encoding the human acrosin-trypsin inhibitor (HUSI-II).

AUTHOR: Moritz A.; Grzeschik K.-H.; Wingender E.; Fink E.

CORPORATE SOURCE: Dept. Clin. Chemistry/Clin. Biochem., University of Munich, Nussbaumstrasse 20,D-8000 Munich 2, Germany

SOURCE: Gene, (1993) 123/2 (277-281).

ISSN: 0378-1119 CODEN: GENED6

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 022 Human Genetics

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A complete cDNA encoding the acrosin-trypsin inhibitor, HUSI-II, was used as a probe to isolate genomic clones from a human placenta library. Three clones which cover the entire HUSI-II gene were isolated and characterized. The exon-intron organization of the gene was determined and found to be identical to other known Kazal-type inhibitor encoding genes. The striking similarity in the amino acid sequences which was found previously in HUSI-II and glycoprotein hormone .beta.-subunits, is neither reflected in codon usage nor in the exon-intron arrangement of the genes. A 1.8-kb segment 5' of the gene was sequenced. The analysis of this sequence showed that HUSI-II contains a G+C-rich region upstream from the transcription start point (tsp) which fulfills the criteria for a CpG island. Furthermore, in the first intron, a potential glucocorticoid-responsive element was found as a half-palindrome flanked by two CACCC elements. Determination of the tsp by S1 mapping revealed that HUSI-II has multiple tsp. Genomic Southern hybridization was used to show that HUSI-II is a single-copy gene. The localization of the gene to chromosome 4 was determined by hybridization of a 5' genomic fragment to the DNA of a panel of somatic hybrids between human and rodent cells.

L210 ANSWER 34 OF 67 USPATFULL

ACCESSION NUMBER: 92:49128 USPATFULL

TITLE: Modified **human** pancreatic secretory **trypsin inhibitor**

INVENTOR(S): Yoshida, Nobuo, Nishinomiya, Japan  
Kikuchi, Norihisa, Takatsuki, Japan  
Shin, Masaru, Kobe, Japan  
Teraoka, Hiroshi, Sakai, Japan

PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Osaka, Japan (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5122594		19920616
APPLICATION INFO.:	US 1989-379002		19890712 (7)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1988-181316	19880719
	JP 1988-255580	19881011
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Lacey, David L.	
ASSISTANT EXAMINER:	Ossanna, Nina	
LEGAL REPRESENTATIVE:	Morrison & Foerster	
NUMBER OF CLAIMS:	4	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	11 Drawing Figure(s); 10 Drawing Page(s)	
LINE COUNT:	989	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB DNA sequences encoding modified varieties of human PSTI possessing excellent stability in terms of decreased susceptibility to decomposition by proteolytic enzymes such as trypsin, as compared with natural human PSTI, as well as the modified varieties of human PSTI obtained by the expression of the DNA sequences.

L210 ANSWER 35 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 1993-402585 [50] WPIDS  
 DOC. NO. CPI: C1993-179265  
 TITLE: New strain of hybrid cells *Mus musculus* L - can be used for prodn. of monoclonal antibodies to acid-stable **trypsin inhibitor** from **human** urine.  
 DERWENT CLASS: B04 D16  
 INVENTOR(S): MARIO, B; OGLOBLINA, O G; RALPH, B  
 PATENT ASSIGNEE(S): (AMCA-R) A MED CARDIOLOGY RES CENTRE  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
SU 1778183	A1	19921130	(199350)*		5

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
SU 1778183	A1	SU 1990-4879754	19901102

PRIORITY APPLN. INFO: SU 1990-4879754 19901102

AB SU 1778183 A UPAB: 19940203

New strain of hybrid cultivable cells *Mus musculus* L, producing monoclonal antibodies to trypsin-binding part of acid-stable **trypsin inhibitor** from **human** urine, is stored in National Collection of cell cultures under No. VSKK/P/505D.

New strain is obtd. by **hybridisation** of splenocytes of mouse Balb/c with mouse myeloma cells P301. Secretion of monoclonal antibodies on the 4th day of culturing in vitro reaches 10-25 micro-g/ml and in ascitic liq. 5-10 mg/ml. Monoclonal antibodies refer to IgG1. Stable prodn. of antibodies continues for 40 passages in vitro and in vivo.

USE/ADVANTAGE - New strain can be used in biotechnology, biology and medicine, in tests for acid-stable **trypsin inhibitor** of **human** urine in biological liquids. Bul.44/30.11.92



Dwg. 0/0

L210 ANSWER 36 OF 67 USPATFULL  
 ACCESSION NUMBER: 91:40475 USPATFULL  
 TITLE: Cytotoxic T lymphocyte serine esterase and method for stimulation and inhibition  
 INVENTOR(S): Pasternack, Mark S., Brookline, MA, United States  
 Eisen, Herman S., Waban, MA, United States  
 PATENT ASSIGNEE(S): Massachusetts Institute of Technology, Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5017489		19910521
APPLICATION INFO.:	US 1988-234906		19880822 (7)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Weimar, Elizabeth C.		
ASSISTANT EXAMINER:	Patterson, Charles L.		
LEGAL REPRESENTATIVE:	Kilpatrick & Cody		
NUMBER OF CLAIMS:	12		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)		
LINE COUNT:	1025		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Antibodies, nucleic acid sequences, and methods for inhibition of lysis for a novel serine esterase produced by both murine and **human** cytotoxic T lymphocytes. The serine esterase has an apparent molecular weight of approximately 28,000-31,000, as determined by SDS gel electrophoresis under reducing conditions, and **trypsin**-like activity. **Inhibition** of the esterase correlates with inhibition of the cells' cytolytic activity. Specific inhibition of the serine esterase is useful as a method for immunosuppression as well as for the inhibition of cytolytic activity of T lymphocytes, both in vivo and in vitro. The genes encoding the murine and **human** serine esterase are **homologous**.

L210 ANSWER 37 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 1991-059025 [09] WPIDS  
 DOC. NO. CPI: C1991-024917  
 TITLE: New polypeptide derivs. of **human** tissue plasminogen activator - used to treat thrombosiscid, prepd. from animal waste and legumes, using process heat to destroy **trypsin inhibitor**.  
 DERWENT CLASS: B04  
 INVENTOR(S): BALDINGER, V; MULLERNEUM, M; SCHMIDT, M; SCHWARZ, M; STRUBE, K H  
 PATENT ASSIGNEE(S): (BADI) BASF AG  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 3930099	A	19910221	(199109)*		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 3930099	A	DE 1989-3930099	19890909

PRIORITY APPLN. INFO: DE 1989-3926039 19890807; DE 1989-3930099  
19890909

AB DE 3930099 A UPAB: 19930928

(I) has one or two extra amino acids substd. or inserted in the 277-527th aminoacid region. Also claimed is a DNA sequence that codes for (I) and vectors contg. the appropriate gene sequence. The DNA sequence can be cloned from human uterine tissue, by isolating mRNA and transcribing into double-stranded cDNA. After inserting the cDNA into the conventional cloning vector pUC9, a cDNA library is built up. The cDNA clone can be isolated.

USE/ADVANTAGE - In the treatment of thrombolysis, (I) has an improved clotting specificity, longer half life, lower inhiBitOr binding and/or h\*gher proteolytic activity than unmodified human tissue plasminogen activator.

0/9

L210 ANSWER 38 OF 67 MEDLINE

ACCESSION NUMBER: 91093294 MEDLINE

DOCUMENT NUMBER: 91093294 PubMed ID: 1985973

TITLE: Molecular cloning and sequence analysis of cDNAs coding for guinea pig alpha 1-antiproteinases S and F and contrapsin.

AUTHOR: Suzuki Y; Yoshida K; Honda E; Sinohara H

CORPORATE SOURCE: Department of Biochemistry, School of Medicine, Kinki University, Osaka, Japan.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Jan 15) 266 (2) 928-32.

Journal code: HIV; 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-M38571; GENBANK-M38572; GENBANK-M38573;

GENBANK-M57269; GENBANK-M57270; GENBANK-M57271;

GENBANK-M57624; GENBANK-M60203; GENBANK-M60204;

GENBANK-M60205; GENBANK-M60206; GENBANK-M62780;

GENBANK-M63262

ENTRY MONTH: 199102

ENTRY DATE: Entered STN: 19910322

Last Updated on STN: 19910322

Entered Medline: 19910212

AB The cDNAs encoding two isoforms, S (slow) and F (fast), of alpha 1-antiproteinase (also referred to as alpha 1-antitrypsin or alpha 1-proteinase inhibitor) as well as contrapsin were obtained by screening lambda gt11 cDNA library prepared fro inflamed guinea pig liver. The sequence analyses of these cDNAs and NH2-terminal peptides of the purified proteins revealed that both isoforms of alpha 1-antiproteinase consist of 405 amino acid residues including a signal peptide of 24 residues and that contrapsin consists of 410 amino acid residues with the same length of the signal peptide. Guinea pig contrapsin had 89, 88, 62, 42, and 41% homology to its own alpha 1-antiproteinases F and S, rat alpha 1-antiproteinase, mouse and rat contrapsins, respectively. This suggests that guinea pig contrapsin is not orthologous to mouse and rat contrapsins and that it developed from a much later duplication of alpha 1-antiproteinase gene after the guinea pig had diverged from the murine lineage. The available data suggest that the reactive site region of alpha 1-antiproteinase can be categorized into orthodox and unorthodox types: the former has P3-P'3 consensus sequence of Xaa-Pro-Met-Ser-Xaa-Pro, where Xaa is Leu, Ile, Val, or Met, while the latter, which occurs in species having multiple alpha

1-antiproteinase isoforms, has the sequence whose P1 Met has changed to other amino acids. Thus, the reactive site region of the orthodox type, which occurs in all seven mammals examined to date, is highly conserved. This is in marked contrast to the fact that the same region is hypervariable among the paralogous proteins belonging to the serpin superfamily.

L210 ANSWER 39 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 1990-024493 [04] WPIDS  
 DOC. NO. CPI: C1990-010787  
 TITLE: Vampire bat glycosylated plasminogen activating protein - which needs fibrin co-factor to activate plasminogen has greater selectivity for fibrin-bound plasminogen than T-pa.  
 DERWENT CLASS: B04 D16  
 INVENTOR(S): DAUGHERTY, B L; DIXON, R A F; DUONG, L T; FRIEDMAN, P A; GARDELL, S J; JACOBS, J W; MARK, G E; JACOBS, J J  
 PATENT ASSIGNEE(S): (MERI) MERCK & CO INC; (SCHD) SCHERING AG  
 COUNTRY COUNT: 25  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 352119	A	19900124	(199004)*	EN	36
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
PT 91236	A	19900208	(199009)		
AU 8938915	A	19900125	(199010)		
NO 8902976	A	19900212	(199012)		
FI 8903500	A	19900121	(199018)		
ZA 8905528	A	19900425	(199022)		
DK 8903575	A	19900123	(199030)		
JP 02167075	A	19900627	(199032)		
EP 352119	B1	19950809	(199536)	EN	84
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
IL 91059	A	19950629	(199538)		
DE 68923741	E	19950914	(199542)		
FI 9503849	A	19950815	(199544)		
ES 2076965	T3	19951116	(199551)		
IE 69054	B	19960807	(199645)		
NO 9700603	A	19900122	(199719)		
FI 100403	B1	19971128	(199802)		
FI 100406	B1	19971128	(199802)		
JP 2713467	B2	19980216	(199812)		31
NO 302954	B1	19980511	(199825)		
US 5830849	A	19981103	(199851)		
KR 134823	B1	19980414	(200011)		
KR 138997	B1	19980430	(200013)		
CA 1341090	C	20000829	(200051)	EN	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 352119	A	EP 1989-307411	19890720
ZA 8905528	A	ZA 1989-5528	19890720
JP 02167075	A	JP 1989-188673	19890720
EP 352119	B1	EP 1989-307411	19890720
IL 91059	A	IL 1989-91059	19890720
DE 68923741	E	DE 1989-623741	19890720
		EP 1989-307411	19890720

FI 9503849	A	Div ex	FI 1989-3500	19890719
			FI 1995-3849	19950815
ES 2076965	T3		EP 1989-307411	19890720
IE 69054	B		IE 1989-2354	19890719
NO 9700603	A	Div ex	NO 1989-2976	19890720
			NO 1997-603	19970210
FI 100403	B1		FI 1989-3500	19890719
FI 100406	B1	Div ex	FI 1989-3500	19890719
			FI 1995-3849	19950815
JP 2713467	B2		JP 1989-188673	19890720
NO 302954	B1		NO 1989-2976	19890720
US 5830849	A	CIP of	US 1988-221697	19880720
		Cont of	US 1989-377221	19890713
		Cont of	US 1991-784102	19911028
		Cont of	US 1992-870170	19920416
			US 1995-467966	19950606
KR 134823	B1		KR 1997-39260	19970819
KR 138997	B1		KR 1989-10264	19890720
CA 1341090	C		CA 1989-606185	19890720

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 68923741	E Based on	EP 352119
ES 2076965	T3 Based on	EP 352119
FI 100403	B1 Previous Publ.	FI 8903500
FI 100406	B1 Previous Publ.	FI 9503849
JP 2713467	B2 Previous Publ.	JP 02167075
NO 302954	B1 Previous Publ.	NO 8902976

PRIORITY APPLN. INFO: US 1989-377221 19890713; US 1988-221697  
 19880720; US 1991-784102 19911028; US  
 1992-870170 19920416; US 1995-467966 19950606

AB EP 352119 A UPAB: 19950223

Purified glycosylated plasminogen activating protein (I) is new which: (a) requires a fibrin cofactor to activate plasminogen (PM); (b) catalyses lysis of plasma clots; and (c) is not inhibited by NaCl when in the presence of a fibrin clot; where mol. wt. of (I) by SDS-PAGE of deglycosylated fonus is <50 KD. (1) (I) with 90% **homology** with one of 4 sequences (given in specification), where (I) needs a fibrin cofactor in order to activate PM; (2) **DNA sequences** encoding 2 specified (I) **sequences**, and **DNA sequences** with 90% **homology** with the other 2 specified (I) sequences; (3) a replicable clotting vector contg. (2); (4) purificn. of (I) by: (a) homogenising submandibular glands from *Desmodus rotundus* vampire bats to form a mixt. and centrifuging; (b) clarifying and concentrating the supernatant; (c) applying vetentate to a phosphocellulose cation exchange column and absorbing (I) to the column; (d) electing to obtain (I) fractions; (e) pooling and applying to an affinity column with immobilised *Erythnira trypsin inhibitor*; (f) Factionating (I) by HPLC; and (g) sepg. (I) by SDS-PAGE. (5) antibodies specifically reactive with (I); (6) glycosylated PM activating fusion protein including residues 190-441 (see Fig.), and a heavy chain sequence from t-PA, the protein having greater PM activating activity than t-PA in presence of type-1 PM activating activity inhibitor; and (7) **mammalian** and bacterial cells transfected with (3).

USE/ADVANTAGE - (I) has greater selectivity towards fibrin-bound PM, so may decrease severity and frequency of bleeding diathesis when used for thrombolytic therapy. (I)

0/12  
Dwg.0/12

L210 ANSWER 40 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 1990-024464 [04] WPIDS  
 DOC. NO. CPI: C1990-010772  
 TITLE: Human PSTI modified at arginine 42 and/or 44 - by  
 substitution by glutamine and/or serine to allow  
 trypsin-inhibitory activity.  
 DERWENT CLASS: B04 D16  
 INVENTOR(S): KIKUCHI, N; SHIN, M; TERAOKA, H; YOSHIDA, N  
 PATENT ASSIGNEE(S): (SHIO) SHIONOGI & CO LTD; (SHIO) SHIONOGI SEIYAKU KK;  
 (SHIO) SHIONOGI PHARM CO LTD  
 COUNTRY COUNT: 18  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 352089	A	19900124 (199004)	*	EN	25
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
AU 8937978	A	19900125 (199010)			
JP 02150282	A	19900608 (199029)			
US 5122594	A	19920616 (199227)			21
EP 352089	B1	19940216 (199407)		EN	31
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
DE 68913090	E	19940324 (199413)			
ES 2062006	T3	19941216 (199505)			
JP 07102137	B2	19951108 (199549)			20
CA 1339875	C	19980519 (199831)			
KR 9615745	B1	19961120 (199930)			

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 352089	A	EP 1989-307309	19890719
JP 02150282	A	JP 1988-255580	19881011
US 5122594	A	US 1989-379002	19890712
EP 352089	B1	EP 1989-307309	19890719
DE 68913090	E	DE 1989-613090	19890719
		EP 1989-307309	19890719
ES 2062006	T3	EP 1989-307309	19890719
JP 07102137	B2	JP 1988-255580	19881011
CA 1339875	C	CA 1989-606044	19890718
KR 9615745	B1	KR 1989-10227	19890719

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 68913090	E Based on	EP 352089
ES 2062006	T3 Based on	EP 352089
JP 07102137	B2 Based on	JP 02150282

PRIORITY APPLN. INFO: JP 1988-181316 19880719; JP 1988-255580  
 19881011

AB EP 352089 A UPAB: 19930928  
 Modified human PSTI (pancreatic secretory **trypsin inhibitor** (I)) is disclosed where Arg (42) and/or (44) from the  
 N-terminus of the natural human PSTI amino acid sequence are replaced with

Glu and/or Ser. Also disclosed are: (1) (I) where Arg (42) or (44) are replaced with Glu and/or Ser, respectively; (2) (I) where one of Arg (42) or Arg (44) is/are replaced by Glu or Ser, (II); (3) (I) where Arg (42) is replaced by Glu; (4) (I) where Arg (44) is replaced by Ser; (5) (I) having the sequence shown in fig. 1 or fig. 2; (6) Any **DNA sequence** encoding the above; (7) Use of the above (I) as a therapeutic trypsin inhibitor.

USE - (I) allows a sustained trypsin inhibition effect useful in the clinical treatment of acute pancreatitis.

0/9

L210 ANSWER 41 OF 67 MEDLINE  
 ACCESSION NUMBER: 90148955 MEDLINE  
 DOCUMENT NUMBER: 90148955 PubMed ID: 2302382  
 TITLE: Molecular cloning and primary structure of rat alpha 1-antitrypsin.  
 AUTHOR: Chao S; Chai K X; Chao L; Chao J  
 CORPORATE SOURCE: Department of Pharmacology and Biochemistry, Medical University of South Carolina, Charleston 29425.  
 CONTRACT NUMBER: HL29397 (NHLBI)  
 SOURCE: BIOCHEMISTRY, (1990 Jan 16) 29 (2) 323-9.  
 Journal code: A0G; 0370623. ISSN: 0006-2960.  
 PUB. COUNTRY: United States  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: GENBANK-M32247  
 ENTRY MONTH: 199003  
 ENTRY DATE: Entered STN: 19900601  
 Last Updated on STN: 19900601  
 Entered Medline: 19900326

AB A cDNA clone encoding rat alpha 1-antitrypsin has been isolated from a lambda gt-11 rat liver cDNA library using an antigen-overlay immunoscreening method. The nucleotide sequence of this cDNA clone is 1306 base pairs in length and has a coding region of 1224 base pairs which can be translated into an alpha 1-antitrypsin precursor protein consisting of 408 amino acid residues. The cDNA sequence contains a termination codon, TAA, at position 1162 and a polyadenylation signal sequence, AATAAT, at position 1212. The calculated molecular weight of the translated mature protein is 43,700 with 387 amino acid residues; this differs from purified rat alpha 1-antitrypsin's apparent molecular weight of 54,000 because of glycosylation. Five potential glycosylation sites were identified on the basis of the cDNA sequence. The translated mature protein sequence from the cDNA clone matches completely with the N-terminal 33 amino acids of purified rat alpha 1-antitrypsin, which has an N-terminal Glu. The cDNA encoding rat alpha 1-antitrypsin shares 70% and 80% sequence identity with its human and mouse counterparts, respectively. The reactive center sequence of rat alpha 1-antitrypsin is highly conserved with respect to human alpha 1-antitrypsin, both having Met-Ser at the P1 and P1' residues. Genomic Southern blot analysis yielded a simple banding pattern, suggesting that the rat alpha 1-antitrypsin gene is single-copy. Northern blot analysis using the cDNA probe showed that rat alpha 1-antitrypsin is expressed at high levels in the liver and at low levels in the submandibular gland and the lung. (ABSTRACT TRUNCATED AT 250 WORDS)

L210 ANSWER 42 OF 67 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:38264 CAPLUS  
 DOCUMENT NUMBER: 114:38264  
 TITLE: Amino acid sequence elucidation of human acrosin-trypsin inhibitor (HUSI-II) reveals that

AUTHOR(S): Kazal-type proteinase inhibitors are structurally related to .beta.-subunits of glycoprotein hormones  
 Fink, Edwin; Hehlele-Fink, Christa; Eulitz, Manfred  
 CORPORATE SOURCE: Dep. Clin. Chem. Clin. Biochem., Univ. Munich, Munich, D-8000, Fed. Rep. Ger.  
 SOURCE: FEBS Lett. (1990), 270(1-2), 222-4  
 CODEN: FEBLAL; ISSN: 0014-5793  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The amino acid sequence of the acrosin-trypsin inhibitor HUSI-II from human seminal plasma is presented which unequivocally identifies HUSI-II as being of Kazal-type. In addn., the HUSI-II sequence shows a striking similarity to the middle part of glycoprotein hormone .beta.-subunits thus revealing a hitherto unknown structural and evolutionary relation between Kazal-type inhibitors and glycoprotein hormones.

L210 ANSWER 43 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 1989-025643 [04] WPIDS  
 DOC. NO. CPI: C1989-011390  
 TITLE: **Human pancreatic secretory trypsin inhibitor** - obtd. by recombinant DNA techniques and free from other proteins of **human** origin.  
 DERWENT CLASS: B04 D16  
 INVENTOR(S): KANAMORI, T; MOCHIDA, E; NOBUHARA, M; OGINO, H  
 PATENT ASSIGNEE(S): (MOCH) MOCHIDA PHARM CO LTD; (MORP) MORISHITA PHARM CO LTD  
 COUNTRY COUNT: 13  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 300459	A	19890125 (198904)*	EN	30	
R: AT BE CH DE ES FR GB GR IT LI NL SE					
JP 01027473	A	19890130 (198910)			

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 300459	A	EP 1988-111704	19880720
JP 01027473	A	JP 1987-184556	19870723

PRIORITY APPLN. INFO: JP 1987-184556 19870723

AB EP 300459 A UPAB: 19930923

A **human pancreatic secretory trypsin inhibitor** (PSTI) free of other proteins of **human** origin is claimed. Also claimed is a vector replicable in *E. coli* comprising (a) a **DNA sequence** encoding the **human** PSTI and (b) a promoter, an **SD sequence** and a **DNA sequence** encoding a signal peptide, which function within *E. coli*. Also claimed are transformants of *E. coli* transformed by the vector.

A **DNA sequence** encoding the **human** PSTI may be obtd. by extracting a genomic DNA of a human cell, by synthesising a **human PSTI cDNA** from mRNA extd. from a human cell or by designing the **DNA sequence** encoding the **human** PSTI on the basis of the amino acid sequence of any of the 4 isoinhibitors and chemically synthesising the DNA. Prefd. *E. coli* strains for expressing the protein are lipoprotein-deleted mutant strains.

USE/ADVANTAGE - The **human** PSTI is free of any contaminants associated

with the purified human PSTI from natural sources. It may be used for the prodn. of monoclonal antibody and the diagnosis of various PSTI-associated diseases.

0/8

L210 ANSWER 44 OF 67 MEDLINE

ACCESSION NUMBER: 90114211 MEDLINE  
DOCUMENT NUMBER: 90114211 PubMed ID: 2608068  
TITLE: Organization of the human corticosteroid binding globulin gene and analysis of its 5'-flanking region.  
AUTHOR: Underhill D A; Hammond G L  
CORPORATE SOURCE: Department of Obstetrics and Gynecology, University of Western Ontario, Victoria Hospital, London, Canada.  
SOURCE: MOLECULAR ENDOCRINOLOGY, (1989 Sep) 3 (9) 1448-54.  
Journal code: NGZ; 8801431. ISSN: 0888-8809.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199002  
ENTRY DATE: Entered STN: 19900328  
Last Updated on STN: 19900328  
Entered Medline: 19900215

AB The structure of the human corticosteroid binding globulin (CBG) gene has been determined, and restriction endonuclease maps of human placental DNA and cloned genomic DNA indicate that CBG is encoded by a single gene. The transcription unit for hepatic CBG mRNA comprises five exons distributed over approximately 19 kilobases (kb), and nuclease protection and primer extension studies using human liver RNA demonstrate that the first exon spans 70 base pairs (bp). Typical of many eukaryotic promoters, sequences that resemble TATA and CAAT-box motifs are centered 28 bp and 73 bp upstream from the origin of transcription, respectively. In addition, six highly conserved sequence elements, responsible for efficient, liver-specific expression of the mouse albumin gene, are located within the first 200 bp of the 5'-flanking region. Further analysis of a region (500 bp) immediately 5' of the transcription start site, however, failed to reveal sequences that might correspond to known steroid hormone response elements. When compared to other serine protease inhibitor genes, the organization of the human CBG gene is most closely related to the human alpha 1-proteinase inhibitor and alpha 1-antichymotrypsin genes. It would therefore appear that these proteins are derived from a common ancestral gene, and this supports the concept that they may be functionally related.

L210 ANSWER 45 OF 67 MEDLINE

ACCESSION NUMBER: 89325681 MEDLINE  
DOCUMENT NUMBER: 89325681 PubMed ID: 2568950  
TITLE: Cloning of the pig aminopeptidase N gene. Identification of possible regulatory elements and the exon distribution in relation to the membrane-spanning region.  
AUTHOR: Olsen J; Sjostrom H; Noren O  
CORPORATE SOURCE: Department of Biochemistry C, Panum Institute, University of Copenhagen, Denmark.  
SOURCE: FEBS LETTERS, (1989 Jul 17) 251 (1-2) 275-81.  
Journal code: EUH; 0155157. ISSN: 0014-5793.  
PUB. COUNTRY: Netherlands  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198908



ENTRY DATE: Entered STN: 19900309  
 Last Updated on STN: 20000303  
 Entered Medline: 19890829

AB We have isolated four lambda-phages covering the complete pig aminopeptidase N/CD13 gene. The sequence of 2.85 kbp encompasses 1.18 kbp of the 5' upstream region and 1.67 kbp of the structural gene. In the promoter region we find a TATA box and potential binding sites for CTF-1/NF-1 and AP-2. By sequence comparisons we have found three domains showing similarity to promoter regions of the genes encoding human alpha 1-antitrypsin and human intestinal alkaline phosphatase. The gene sequence includes the first three exons and two introns. It shows that a single exon encodes the cytoplasmic tail, the membrane anchor and the junctional peptide.

L210 ANSWER 46 OF 67 USPATFULL

ACCESSION NUMBER: 88:68916 USPATFULL  
 TITLE: Process for concentrating and separating  
**trypsin inhibitor** and kallidinogenase  
 in **human** urine  
 INVENTOR(S): Yuki, Yoshikazu, Kobe, Japan  
 Nakanishi, Koichiro, Ashiya, Japan  
 Hiratani, Hajime, Sennan, Japan  
 PATENT ASSIGNEE(S): Japan Chemical Research Co., Ltd., Kobe, Japan  
 (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4780209		19881025
APPLICATION INFO.:	US 1987-104634		19871002 (7)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1986-870083, filed on 3 Jun 1986, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Therkorn, Ernest G.		
LEGAL REPRESENTATIVE:	Bryan, Cave, McPheeters & McRoberts		
NUMBER OF CLAIMS:	11		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)		
LINE COUNT:	392		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Two components, trypsin and kallidinogenase, in human urine are concentrated simultaneously by allowing human urine at neutral pH, collecting bubbles thus formed to obtain the concentrate of the two components, adjusting the concentrate to weak acidity, contacting the acidified concentrate with chitosan to allow the two components to be adsorbed onto chitosan, eluting the components from the adsorbent with aqueous ammonia solution, and neutralizing and heating the eluate at about 60.degree. C. for about 10 hours to make the eluate virus-free, followed by separating the components from the eluate.

L210 ANSWER 47 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 1988-133245 [19] WPIDS  
 DOC. NO. CPI: C1988-059638  
 TITLE: **Human pancreatic secretory trypsin inhibitors** - used to prevent and treat diseases resulting in auto digestion of pancreatic tissue.  
 DERWENT CLASS: B04 D16  
 INVENTOR(S): BANDYOPADH, P; EISENBERG, S; KOHNO, T; THOMPSON, R  
 PATENT ASSIGNEE(S): (SYND) SYNERGEN BIOLOGICAL INC  
 COUNTRY COUNT: 30

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8803171	A	19880505	(198819)*	EN	39
RW: AT BE CH DE FR GB IT LU NL OA SE					
W: AT AU BB BG BR CH DE DK FI GB HU JP KP KR LK LU MC MG MW NL NO RO					
SD SE SU					
AU 8781727	A	19880520	(198833)		
DK 8803442	A	19880623	(198846)		
NO 8802843	A	19881017	(198847)		
EP 329693	A	19890830	(198935)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					
JP 02501027	W	19900412	(199021)		
EP 329693	A4	19891115	(199508)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8803171	A	WO 1987-US2585	19871009
EP 329693	A	EP 1987-907369	19871009
JP 02501027	W	JP 1987-506869	19871009
EP 329693	A4	EP 1987-907369	

PRIORITY APPLN. INFO: US 1986-924991 19861030

AB WO 8803171 A UPAB: 19930923

A novel **human** pancreatic secretory **trypsin inhibitor** (HPSTI) comprises a protein possessing at least one active site with the ability to inhibit proteases, where the inhibitor is **homologous** to that isolatable from human pancreatic tissues and where the inhibitor is produced using recombinant DNA methods.

USE/ADVANTAGE - The HPSTI and analogues prepd. by recombinant DNA methods enable improved research into the prevention and treatment of diseases resulting in the autodigestion of pancreatic tissue and are used to prevent the trypsin-catalysed activation of pancreatic proteolytic zymogens. The HPSTI and some analogues are biologically equiv. to HPSTI isolatable from human pancreatic tissues and juices. Other analogues are capable of inhibiting proteolytic enzymes other than trypsin to prevent destruction of various tissues, e.g. elastase which has been implicated in a causative role in emphysema.

0/3

L210 ANSWER 48 OF 67 MEDLINE

ACCESSION NUMBER: 88122641 MEDLINE

DOCUMENT NUMBER: 88122641 PubMed ID: 2893291

TITLE: Novel precursor of Alzheimer's disease amyloid protein shows protease inhibitory activity.

AUTHOR: Kitaguchi N; Takahashi Y; Tokushima Y; Shiojiri S; Ito H

CORPORATE SOURCE: Life Science Research Laboratories, Asahi Chemical Industry Co. Ltd., Shizuoka, Japan.

SOURCE: NATURE, (1988 Feb 11) 331 (6156) 530-2.  
Journal code: NSC; 0410462. ISSN: 0028-0836.

PUB. COUNTRY: ENGLAND: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-X06981

ENTRY MONTH: 198803

ENTRY DATE: Entered STN: 19900308  
Last Updated on STN: 19980206  
Entered Medline: 19880317

AB Alzheimer's disease is characterized by cerebral deposits of amyloid beta-protein (AP) as senile plaque core and vascular amyloid, and a complementary DNA encoding a precursor of this protein (APP) has been cloned from human brain. From a cDNA library of a human glioblastoma cell line, we have isolated a cDNA identical to that previously reported, together with a new cDNA which contains a 225-nucleotide insert. The sequence of the 56 amino acids at the N-terminal of the protein deduced from this insert is highly homologous to the basic trypsin inhibitor family, and the lysate from COS-1 cells transfected with the longer APP cDNA showed an increased inhibition of trypsin activity. Partial sequencing of the genomic DNA encoding APP showed that the 225 nucleotides are located in two exons. At least three messenger RNA species, apparently transcribed from a single APP gene by alternative splicing, were found in human brain. We suggest that protease inhibition by the longer APP(s) could be related to aberrant APP catabolism.

L210 ANSWER 49 OF 67 MEDLINE  
ACCESSION NUMBER: 88314108 MEDLINE  
DOCUMENT NUMBER: 88314108 PubMed ID: 2842251  
TITLE: Molecular structure and sequence homology of a gene related to alpha 1-antitrypsin in the human genome.  
AUTHOR: Bao J J; Reed-Fourquet L; Sifers R N; Kidd V J; Woo S L  
CORPORATE SOURCE: Howard Hughes Medical Institute, Baylor College of Medicine, Houston, Texas 77030.  
CONTRACT NUMBER: HL07343 (NHLBI)  
HL27509 (NHLBI)  
HL37188 (NHLBI)  
SOURCE: GENOMICS, (1988 Feb) 2 (2) 165-73.  
Journal code: GEN; 8800135. ISSN: 0888-7543.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-J03044; GENBANK-M19684; GENBANK-M19685  
ENTRY MONTH: 198810  
ENTRY DATE: Entered STN: 19900308  
Last Updated on STN: 19970203  
Entered Medline: 19881011

AB A 7.7-kb EcoRI genomic DNA fragment highly homologous to the human alpha 1-antitrypsin (AAT) gene has been cloned. This antitrypsin-related sequence is physically linked to the authentic AAT gene and both are present in a single cosmid clone. Nucleotide sequencing of the AAT-related genomic fragment demonstrated extensive homology with the authentic AAT gene in the introns as well as in the exons. The conservation of all RNA splice sites and lack of internal termination codons in the exonic regions suggest that it may not be a classical pseudogene. If expressed, it could result in a protein of 420 amino acid residues exhibiting a 70% overall homology with human alpha 1-antitrypsin. The signal peptide sequence is well conserved in the related gene, but the active site for protease inhibition of Met-Ser in alpha 1-antitrypsin has been changed to Trp-Ser. These data suggest that the putative protein encoded by the AAT-related gene is a secretory serine protease inhibitor with an altered substrate specificity. Interestingly, even the intronic regions in the related gene exhibit a 65% overall nucleotide sequence homology with those of the authentic AAT gene. These results suggest that the AAT-related gene is derived from a recent duplication of the authentic AAT gene and represents a new member of the serine protease inhibitor superfamily.

L210 ANSWER 50 OF 67 WPIDS (C) 2002 THOMSON DERWENT  
 ACCESSION NUMBER: 1986-169458 [26] WPIDS  
 CROSS REFERENCE: 1986-169441 [26]; 1988-227612 [32]; 1999-166640 [14];  
 1999-346413 [29]; 2000-678667 [63]; 2001-637974 [62];  
 2002-121475 [13]  
 DOC. NO. CPI: C1986-072812  
 TITLE: New synthetic **DNA sequences** for  
 directing microbial synthesis - for prodn. of single poly  
 peptide chain serine protease inhibitor having leukocyte  
 elastase and trypsin inhibitory sites.  
 DERWENT CLASS: B04 D16  
 INVENTOR(S): OHLSSON, K; THOMPSON, R C; BANDYOPADH, P K; EISENBERG, S  
 P; STETLER, G L  
 PATENT ASSIGNEE(S): (SYND) SYNERGEN BIOLOGICAL INC  
 COUNTRY COUNT: 19  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8603519	A	19860619	(198626)*	EN	62
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU DK FI HU JP KR NO					
ES 8700691	A	19870116	(198711)		
ZA 8509363	A	19870305	(198721)		
JP 62501262	W	19870521	(198726)		
JP 2672088	B2	19971105	(199749)		30

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8603519	A	WO 1985-US2385	19851204
ES 8700691	A	ES 1985-549630	19851205
ZA 8509363	A	ZA 1985-9363	19851206
JP 62501262	W	JP 1986-500018	19851204
JP 2672088	B2	WO 1985-US2385	19851204
		JP 1986-500018	19851204

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 2672088	B2 Previous Publ. Based on	JP 62501262 WO 8603519

PRIORITY APPLN. INFO: WO 1985-US2385 19851204; US 1984-678822  
 19841206

AB WO 8603519 A UPAB: 20020429

(1) Synthetic **DNA sequence** capable of directing microbial synthesis of a single polypeptide chain serine protease inhibitor (I) having at least one active site possessing serine protease inhibitor activity is new. (I) has good **homology** to the native serin protease inhibitor isolated from parotid secretions. (2) Translational coupler having the **nucleotide sequence** of formula (II) is new. TAA CGA GGC GCA AAA AAT GAA AAA GAC AGC TAT CGC GAT CAA GGA GAA ATA AAT G (II) USE/ADVANTAGE - The **DNA sequence** directs synthesis of (I), which is believed to have at least 2 active sites, one exhibiting leukocyte elastase inhibiting properties and the other exhibiting **inhibitory** activity against

**trypsin.** (I) has good resistance to heat and acids and it is resistant to proteolytic degradation by a variety of proteolytic enzymes. It is also thermodynamically stable under the conditions normally encountered extracellularly in the **mammalian** body. Denatured forms of (I) can also form the disulphide bonds and can form the no-covalent interactions necessary to assume an active tertiary structure in the absence of biochemical stimulus. (I) differs greatly from other known leukocyte elastase inhibitors. It can be prepd. from the **DNA sequence** in quantities and amts. sufficient for economic use.  
Dwg.0/4

L210 ANSWER 51 OF 67 MEDLINE  
 ACCESSION NUMBER: 86120356 MEDLINE  
 DOCUMENT NUMBER: 86120356 PubMed ID: 3003690  
 TITLE: A new member of the plasma protease inhibitor gene family.  
 AUTHOR: Ragg H  
 SOURCE: NUCLEIC ACIDS RESEARCH, (1986 Jan 24) 14 (2) 1073-88.  
 Journal code: O8L; 0411011. ISSN: 0305-1048.  
 PUB. COUNTRY: ENGLAND: United Kingdom  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 OTHER SOURCE: GENBANK-X03498  
 ENTRY MONTH: 198603  
 ENTRY DATE: Entered STN: 19900321  
 Last Updated on STN: 19900321  
 Entered Medline: 19860321

AB A 2.1-kb cDNA clone representing a new member of the protease inhibitor family was isolated from a human liver cDNA library. The inhibitor, named human Leuserpin 2 (hLS2), comprises 480 amino acids and contains a leucine residue at its putative reactive center. HLS2 is about 25-28% homologous to three human members of the plasma protease inhibitor family: antithrombin III, alpha 1-antitrypsin and alpha 1-antichymotrypsin. A comparison with published partial amino acid sequences shows that hLS2 is closely related to the thrombin inhibitor heparin cofactor II.

L210 ANSWER 52 OF 67 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1985:418949 CAPLUS  
 DOCUMENT NUMBER: 103:18949  
 TITLE: Human inter-.alpha.-trypsin inhibitor: localization of the Kunitz-type domains in the N-terminal part of the molecule and their release by a trypsin-like proteinase  
 AUTHOR(S): Reisinger, Peter; Hochstrasser, Karl; Albrecht, Gerd J.; Lempart, Kathrin; Salier, Jean Philippe  
 CORPORATE SOURCE: Klin. Poliklin. Hals-, Nasen- Ohrenkranke, Univ. Muenchen, Munich, D-8000/70, Fed. Rep. Ger.  
 SOURCE: Biol. Chem. Hoppe-Seyler (1985), 366(5), 479-83  
 CODEN: BCHSEI  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The N-terminal amino acid sequence of human inter-.alpha.-trypsin inhibitor (ITI) is identical with that of the acid-stable human 30-kilodalton inhibitors (HI-30) from urine and serum and with those released from inter-.alpha.-trypsin inhibitor by trypsin or chymotrypsin. Serum HI-30 and HI-30 released by trypsin differ from the urinary inhibitor by an addnl. C-terminal arginine residue. Compared to these 2 inhibitors, the inhibitor released by chymotryptic proteolysis is elongated C-terminally by an addnl. phenylalanine residue. HI-30 thus appears to be the N-terminus of the inter-.alpha.-trypsin inhibitor,

released from this inhibitor in vivo by cleavage of the Arg123-Phe124 peptide bond by trypsinlike proteinases.

L210 ANSWER 53 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1985:518718 CAPLUS

DOCUMENT NUMBER: 103:118718

TITLE: Studies on the protease inhibitors in lung cancer tissue. I. Purification of urinary trypsin inhibitor-like inhibitor from human lung cancer tissue

AUTHOR(S): Okumichi, Tsuneo

CORPORATE SOURCE: Sch. Med., Hiroshima Univ., Hiroshima, 734, Japan

SOURCE: Hiroshima Daigaku Igaku Zasshi (1985), 33(1), 1-16

CODEN: HDIZAB; ISSN: 0018-2087

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB Trypsin-inhibitory activity was significantly higher in exts. from human lung cancer tissue than in that from normal lung tissue. The antigenicity of the inhibitor in the lung cancer tissue was the same as that of urinary trypsin inhibitor as detd. by double immunodiffusion, immunoelectrophoresis, and neutralization with rabbit anti-(urinary trypsin inhibitor) IgG. The mol. wt. of the lung cancer trypsin inhibitor was .apprx.67,000 in gel filtration. The inhibitor was sepd. into 2 bands with mol. wt. of 43,000 and 20,000 on SDS-polyacrylamide gel electrophoresis (SDS-PAGE). From 1 g of lung cancer tissue, 20-60 .mu.g of the inhibitor, with a specific activity of 2,000 units/mg protein was obtained by the SDS-PAGE method. The lung cancer trypsin inhibitor markedly inhibited trypsin, chymotrypsin, and kallikrein, and weakly inhibited plasmin, but it did not inhibit urokinase, thrombin, or collagenase.

L210 ANSWER 54 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1984:402886 CAPLUS

DOCUMENT NUMBER: 101:2886

TITLE: Isolation of two novel proteinase inhibitors from hemolymph of silkworm larva, Bombyx mori. Comparison with human serum proteinase inhibitors

AUTHOR(S): Sasaki, Takuji; Kobayashi, Kazuto

CORPORATE SOURCE: Sch. Agric., Nagoya Univ., Nagoya, 464, Japan

SOURCE: J. Biochem. (Tokyo) (1984), 95(4), 1009-17

CODEN: JOBIAO; ISSN: 0021-924X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two protein proteinase inhibitors, antitrypsin and antichymotrypsin, were isolated from the hemolymph of silkworm larva, B. mori, using conventional gel filtration and ion-exchange chromatog. techniques. They had similar physicochem. properties, e.g. mol. wt. (42,000 for antitrypsin and 43,000 for antichymotrypsin), amino acid compn., and CD spectrum. Further comparison of these characteristics with human serum inhibitors, .alpha.-1-proteinase inhibitor and .alpha.-1-antichymotrypsin, suggested the resemblance of silkworm and human inhibitors. The N-terminal sequences were not, however, homologous to each other, and antiserum against each silkworm inhibitor only formed a precipitin line with its own antigen. Differences in minute parts of the inhibitors are indicated.

L210 ANSWER 55 OF 67 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:120615 CAPLUS

DOCUMENT NUMBER: 98:120615

TITLE: The human .alpha.1-antitrypsin gene: its sequence homology and structural comparison with the chicken ovalbumin gene

AUTHOR(S): Woo, Savio L. C.; Chandra, T.; Kidd, Vincent J.; Long, George L.; Kurachi, Kotoku; Davie, Earl W.  
 CORPORATE SOURCE: Howard Hughes Med. Inst. Lab., Baylor Coll. Med., Houston, TX, 77030, USA  
 SOURCE: UCLA Symp. Mol. Cell. Biol. (1982), 26(Gene Regul.), 55-64  
 CODEN: USCBDO  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Genomic .alpha.-antitrypsin [9035-81-8] DNA clones were isolated from a **human** DNA library with an .alpha.1-antitrypsin cDNA clone from baboon as hybridization probe; the mol. structure of the **human** gene was examd. by hybridization with .alpha.-1 antitrypsin-specifying mRNA of baboon and electron microscopy of hybrids. The screening of 2 .times. 106 plaques from the **human** genomic DNA library yielded 16 independent phage isolates which originated from 4 independent clones, designated .alpha.AT135, .alpha.AT35, .alpha.AT80, and .alpha.AT101. Hybridization of the **human** genomic DNA and baboon mRNA showed that the gene contained exon regions I, II, III, and IV of 0.71, 0.33, 0.13, and 0.27 kilobases and introns A, B, and C of 1.45, 1.15, and 0.8 kilobases. The 9.6-kilobase EcoRI DNA fragment contg. the **human** gene was subcloned into the EcoRI site of plasmid pBR322; the resulting plasmid, pAT 9.6, was examd. by restriction mapping and Southern hybridization. The presence of 4 exons and 3 introns within the gene was confirmed. The **human** .alpha.1-antitrypsin gene shared significant sequence homol. with the chick ovalbumin gene, but the no., positions, and sizes of the intervening sequences differed. The evolutionary origin of the 2 genes is discussed.

L210 ANSWER 56 OF 67 USPATFULL

ACCESSION NUMBER: 75:54506 USPATFULL  
 TITLE: Protease inhibitor from horse urine  
 INVENTOR(S): Singh, Kartar, Beaconsfield, Canada  
 PATENT ASSIGNEE(S): Ayerst, McKenna and Harrison Ltd., Montreal, Canada (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3912704		19751014
APPLICATION INFO.:	US 1974-469180		19740513 (5)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1972-251168, filed on 8 May 1972, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Schain, Howard E.		
NUMBER OF CLAIMS:	1		
EXEMPLARY CLAIM:	1		
LINE COUNT:	548		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A protease inhibitor isolated from horse urine particularly active against trypsin, chymotrypsin and plasmin which differs from a **similar** inhibitor isolated from **human** urine in having a different isoelectric point, different staining properties, and about twice the **trypsin-inhibiting** activity of the latter, and a process for isolating the said protease inhibitor from horse urine.

L210 ANSWER 57 OF 67 MEDLINE  
 ACCESSION NUMBER: 74147535 MEDLINE  
 DOCUMENT NUMBER: 74147535 PubMed ID: 4274689

TITLE: Treatment of chronic urticaria with a proteinase  
(kallikrein) inhibitor.  
AUTHOR: Berova N; Petkov I; Andreev V C  
SOURCE: BRITISH JOURNAL OF DERMATOLOGY, (1974 Apr) 90 (4) 431-4.  
Journal code: AW0; 0004041. ISSN: 0007-0963.  
PUB. COUNTRY: ENGLAND: United Kingdom  
(CLINICAL TRIAL)  
(CONTROLLED CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 197406  
ENTRY DATE: Entered STN: 19900310  
Last Updated on STN: 20000303  
Entered Medline: 19740619

L210 ANSWER 58 OF 67 MEDLINE  
ACCESSION NUMBER: 74157850 MEDLINE  
DOCUMENT NUMBER: 74157850 PubMed ID: 4545256  
TITLE: Interaction of human serum proteinase inhibitors with  
proteolytic enzymes of animal, plant, and bacterial origin.  
AUTHOR: Sasaki M; Yamamoto H; Iida S  
SOURCE: JOURNAL OF BIOCHEMISTRY, (1974 Jan) 75 (1) 171-7.  
Journal code: HIF; 0376600. ISSN: 0021-924X.  
PUB. COUNTRY: Japan  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 197407  
ENTRY DATE: Entered STN: 19900310  
Last Updated on STN: 19900310  
Entered Medline: 19740705

L210 ANSWER 59 OF 67 MEDLINE  
ACCESSION NUMBER: 74091289 MEDLINE  
DOCUMENT NUMBER: 74091289 PubMed ID: 4130044  
TITLE: Serum protein profiles in thermal burns. II. Protease  
inhibitors, complement factors, and c-reactive protein.  
AUTHOR: Daniels J C; Larson D L; Abston S; Ritzmann S E  
SOURCE: JOURNAL OF TRAUMA, (1974 Feb) 14 (2) 153-62.  
Journal code: KAF; 0376373. ISSN: 0022-5282.  
PUB. COUNTRY: United States  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 197404  
ENTRY DATE: Entered STN: 19900310  
Last Updated on STN: 19900310  
Entered Medline: 19740402

L210 ANSWER 60 OF 67 MEDLINE  
ACCESSION NUMBER: 73000150 MEDLINE  
DOCUMENT NUMBER: 73000150 PubMed ID: 4262591  
TITLE: Human skin proteases.  
AUTHOR: Fraki J E; Hopsu-Havu V K  
SOURCE: ARCHIV FUR DERMATOLOGISCHE FORSCHUNG, (1972) 243 (3)  
153-63.  
Journal code: 6X5; 7512588. ISSN: 0003-9187.  
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of  
Journal; Article; (JOURNAL ARTICLE)



LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 197211  
ENTRY DATE: Entered STN: 19900310  
Last Updated on STN: 19900310  
Entered Medline: 19721108

## L210 ANSWER 61 OF 67 MEDLINE

ACCESSION NUMBER: 72112495 MEDLINE  
DOCUMENT NUMBER: 72112495 PubMed ID: 4536746  
TITLE: [Comparison of the effects of proteinase inhibitors antilysin, contrycal and trasylol on trypsin and chymotrypsin activity in man].  
Srovnani ucinku proteinazovych inhibitoru Antilysinu, Contrykalu a Trasylolu na trypsinovou a chymotrypsinovou aktivitu cloveka.  
AUTHOR: Malis F; Fric P; Slezak Z  
SOURCE: CESKOSLOVENSKA GASTROENTEROLOGIE A VYZIVA, (1972 Jan) 26 (1) 12-7.  
Journal code: CTK; 0402356. ISSN: 0009-0565.  
PUB. COUNTRY: Czechoslovakia  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: Czech  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 197204  
ENTRY DATE: Entered STN: 19900310  
Last Updated on STN: 19900310  
Entered Medline: 19720428

## L210 ANSWER 62 OF 67 MEDLINE

ACCESSION NUMBER: 71234464 MEDLINE  
DOCUMENT NUMBER: 71234464 PubMed ID: 4253726  
TITLE: Studies of kallikrein inhibitors in potatoes. II. Effect of potato kallikrein inhibitors on various kallikreins and other proteases.  
AUTHOR: Hojima Y; Moriya H; Moriwaki C  
SOURCE: JOURNAL OF BIOCHEMISTRY, (1971 Jun) 69 (6) 1027-32.  
Journal code: HIF; 0376600. ISSN: 0021-924X.  
PUB. COUNTRY: Japan  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 197108  
ENTRY DATE: Entered STN: 19900101  
Last Updated on STN: 20000303  
Entered Medline: 19710821

## L210 ANSWER 63 OF 67 MEDLINE

ACCESSION NUMBER: 72025013 MEDLINE  
DOCUMENT NUMBER: 72025013 PubMed ID: 4939580  
TITLE: [Physiopathology and clinical picture of hereditary antiproteinase deficiency syndromes].  
Pathophysiologie und Klinik hereditarer Antiproteinasen-Mangelsyndrome.  
AUTHOR: Duck H J  
SOURCE: ZEITSCHRIFT FUR DIE GESAMTE INNERE MEDIZIN UND IHRE GRENZGEBIETE, (1971 Jul 15) 26 (14) 445-51. Ref: 107  
Journal code: XUY; 21730470R. ISSN: 0044-2542.  
PUB. COUNTRY: GERMANY, EAST: German Democratic Republic  
Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)  
LANGUAGE: German  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 197112  
ENTRY DATE: Entered STN: 19900310  
Last Updated on STN: 19900310  
Entered Medline: 19711230

L210 ANSWER 64 OF 67 MEDLINE  
ACCESSION NUMBER: 71130810 MEDLINE  
DOCUMENT NUMBER: 71130810 PubMed ID: 5313313  
TITLE: The kinin-system of human plasma. I. Isolation of a low molecular weight activator of prekallikrein.  
AUTHOR: Movat H Z; Poon M C; Takeuchi Y  
SOURCE: INTERNATIONAL ARCHIVES OF ALLERGY AND APPLIED IMMUNOLOGY, (1971) 40 (1) 89-112.  
Journal code: GP9; 0404561. ISSN: 0020-5915.  
PUB. COUNTRY: Switzerland  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 197104  
ENTRY DATE: Entered STN: 19900101  
Last Updated on STN: 20000303  
Entered Medline: 19710420

L210 ANSWER 65 OF 67 MEDLINE  
ACCESSION NUMBER: 70182221 MEDLINE  
DOCUMENT NUMBER: 70182221 PubMed ID: 5309810  
TITLE: [Influence of Trasylol on the effect of various proteases on erythrocytes].  
Uber den Einfluss von Trasylol bezüglich der Wirkung von verschiedenen Proteasen auf Erythrocyten.  
AUTHOR: Uhlenbruck G; Wintzer G  
SOURCE: KLINISCHE WOCHENSCHRIFT, (1969 Jun 15) 47 (12) 673-5.  
Journal code: KWH; 2985205R. ISSN: 0023-2173.  
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: German  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 197006  
ENTRY DATE: Entered STN: 19900101  
Last Updated on STN: 20000303  
Entered Medline: 19700624

L210 ANSWER 66 OF 67 MEDLINE  
ACCESSION NUMBER: 68090073 MEDLINE  
DOCUMENT NUMBER: 68090073 PubMed ID: 4229180  
TITLE: In vitro and in vivo studies with trasylol, an anticoagulant and a fibrinolytic inhibitor.  
AUTHOR: Dubber A H; McNicol G P; Uttley D; Douglas A S  
SOURCE: BRITISH JOURNAL OF HAEMATOLOGY, (1968 Jan) 14 (1) 31-49.  
Journal code: AXC; 0372544. ISSN: 0007-1048.  
PUB. COUNTRY: ENGLAND: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 196802  
ENTRY DATE: Entered STN: 19900101  
Last Updated on STN: 19970203

Entered Medline: 19680214

L210 ANSWER 67 OF 67 MEDLINE  
ACCESSION NUMBER: 68099678 MEDLINE  
DOCUMENT NUMBER: 68099678 PubMed ID: 5299789  
TITLE: [On the mechanism of the effect of various inhibitors of  
fibrinolysis].  
K mechanismu ucinku nekterych inhibitoru fibrinolzy.  
AUTHOR: Donner L; Houskova J  
SOURCE: SBORNIK LEKARSKY, (1967) 69 (11) 343-51.  
Journal code: UAW; 0025770. ISSN: 0036-5327.  
PUB. COUNTRY: Czechoslovakia  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: Czech  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 196802  
ENTRY DATE: Entered STN: 19900101  
Last Updated on STN: 19900101  
Entered Medline: 19680226